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# **THE CHEMISTRY OF SILYLAZIRIDINES**

**Thesis submitted by  
Patricia Ann Kyle B.Sc. (Glasgow)  
for the degree of  
Doctor of Philosophy  
May 1993**

**Department of Chemistry  
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# Contents

Title page	i
Acknowledgements	ii
Declaration	iii
Contents	iv
Abstract	xi

## Chapter 1: Introduction 1

1.1	Introduction to organosilicon chemistry	1
1.1.1	Preliminary considerations	1
1.1.2	Physical properties of organosilanes	1
1.1.3	Directive effects of the silyl group	5
1.2	The synthetic utility of 2-silylated heterocycles	5
1.2.1	Some chemistry of 3-membered heterocycles	5
1.2.2	Introduction to the chemistry of silylepoxides	7
1.2.3	Reactions of silylepoxides involving ring cleavage	8
1.2.4	$\alpha$ -Deprotonation-metalation of silylepoxides	11
1.2.5	2-Trimethylsilylaziridines as synthetic intermediates	13
1.3	Synthesis of 2-silylaziridines	15
1.3.1	Syntheses of silylaziridines by the reaction of arylazides with vinylsilanes	15
1.3.2	Syntheses of silylaziridines by the reduction of silylhaloazides	19
1.3.3	Syntheses of silylaziridines by cyclization of silylated chlorocarbamates	21
1.3.4	Syntheses of silylaziridines by the reaction of a quinazolone nitrene with vinylsilanes	24
1.3.5	Syntheses of silylaziridines by the reaction of $\alpha$ -silyl carbanions with imines	26
1.4	References	30

## Chapter 2: Silylaziridines: New synthetic methods 34

2.1	Introduction	34
2.1.1	Previous syntheses of silylaziridines	34
2.1.2	New routes to silylaziridines	35
2.2	Preparative and mechanistic aspects of silylaziridine synthesis	36
2.2.1	The thermal reaction of phenyl azide in the presence of vinylsilanes	36
2.2.2	The preparation of silylaziridines by reduction of silylsubstituted bromoazides	43

2.2.2.1 Stereocontrol in the synthesis of diastereoisomeric bromoazides from <i>trans</i> -trimethylsilylstyrene	44
2.2.2.2 Synthesis of other silylbromoazide adducts	50
2.2.3 Synthesis of silylaziridines by the photochemical decomposition of alkyl azidoformates in the presence of vinylsilanes.	55
2.2.4 Silylaziridines formed by ring preserving reactions of parent silylaziridines	59
2.3 References	61
 <b>Chapter 3: Reactivity of silylaziridines</b>	 63
3.1 Introduction	63
3.2 Reactions involving ring cleavage - preliminary considerations	63
3.2.1 Ring opening of aziridines with nucleophilic reagents	65
3.2.2 Ring opening of aziridines with electrophilic reagents	66
3.2.3 Ring opening reactions of 2-silyl substituted aziridines and epoxides	68
3.2.4 Spectroscopic evidence for the direction of ring opening	70
3.3 Ring opening reactions of silylaziridines with hydrogen halides	72
3.3.1 Introduction	72
3.3.2 Reaction of 1-carboethoxysilylaziridines with hydrogen halides	72
3.3.3 Reaction of $\alpha$ -carbomethoxyaziridines with hydrogen halides	75
3.3.4 Reaction of <i>N</i> -unsubstituted silylaziridines with hydrogen halides	76
3.4 Ring opening reactions with triflates	77
3.5 Ring opening reactions with trifluoroacetic acid	83
3.6 Ring opening of silylaziridines with trimethylsilyl halides	84
3.7 Reactions of silylaziridines and silylepoxides with nucleophilic reagents	88
3.7.1 Introduction	88
3.7.2 Nucleophilic ring opening reactions of silylepoxides	90
3.7.3 Competition between ring opening and reaction at a carbonyl group	92
3.7.4 SET mechanism in aziridine ring cleavage	95
3.7.5 Reaction of silylaziridines with nucleophilic reagents	96
3.8 References	98
 <b>Chapter 4: Fluorodesilylation of silylaziridines</b>	 101
4.1 Introduction	101
4.2 Fluoride ion induced desilylation	101

4.3	Sources of fluoride ion and problems with their use	104
4.3.1	Introduction	105
4.3.3	Availability of sources of fluoride ion	106
4.4	Fluorodesilylation of silylaziridines	107
4.5	Mechanism of fluorodesilylation of silylaziridines	118
4.6	Spectroscopic features	124
4.7	Conclusions	127
4.8	References	128
 <b>Chapter 5: Conjugate addition reactions of some vinylsilanes</b>		<b>130</b>
5.1	Introduction	130
5.1.1	Initial aims of the project	131
5.2	The role of silicon in promoting the Michael reaction	134
5.3	Previous reactions involving $\alpha$ -lithiovinyltrialkylsilanes and carbonyl compounds	136
5.3.1	General aspects of the Michael addition reaction	136
5.3.2	Reactions involving Michael addition-Peterson olefination	138
5.4	Experimental aspects of the Michael addition reactions	139
5.4.1	Introduction	139
5.4.2	Experimental conditions	140
5.5	Mechanistic aspects of the reactions of $\alpha$ -lithiovinyltrimethylsilane with carbonyl compounds	143
5.5.1	Overview of the chemistry involved	143
5.5.2	1,2 Versus 1,4 addition	143
5.5.3	The reaction of $\alpha$ -lithiovinyltrimethylsilane with ethyl chloroformate	146
5.5.4	The reaction of ethyl acetate with $\alpha$ -lithiovinyltrimethylsilane	148
5.5.5	Carbon versus oxygen alkylation	152
5.5.6	Reaction of $\alpha$ -lithiovinyltrimethylsilane with acetic anhydride	154
5.5.7	Reaction of $\alpha$ -lithiovinyltrimethylsilane with dimethylcarbonyl chloride	154
5.5.8	Reaction of $\alpha$ -lithiovinyltrimethylsilane with phenyl chloroformate	155
5.6	Spectroscopic features	156
5.7	Conclusions	157



5.8	References	159
<b>Chapter 6:</b>	<b>Experimental</b>	<b>160</b>
Measurement of data		160
Handling of moisture sensitive compounds		161
Sources and Purification of reagents		161
1. Solvents		161
2. Purification of starting materials		162
Synthesis of starting materials		163
6.1	Preparation of trimethylsilylbromoazides from vinylsilanes (method A)	165
(i)	RS/SR-2-azido-1-bromo-2-phenyl-1-trimethylsilylethane	165
(ii)	2-Azido-1-bromo-1-triphenylsilylethane	166
(iii)	Bis(2-azido-1-bromoethyl)dimethylsilane	166
6.2.	Preparation of trimethylsilylbromoazides from vinylsilanes (method B)	167
(i)	SS/RR-2-azido-1-bromo-2-phenyl-1-trimethylsilylethane	167
(ii)	2-Azido-1-bromo-1-trimethylsilylhexane	167
6.3	Procedure for the lithium aluminium hydride reduction of silylbromoazides to the corresponding silylaziridines	168
(i)	<i>Cis</i> -3-phenyl-2-trimethylsilylaziridine	168
(ii)	<i>Trans</i> -3-phenyl-2-trimethylsilylaziridine	169
(iii)	Attempted reduction of bis(2-azido-1-bromoethyl)dimethylsilane, synthesis of dimethyl di(2-amino ethyl)silane	169
(iv)	2-Triphenylsilylaziridine	169
6.4.	Reductions of 2-azido-1-bromo-1-trimethylsilylhexane	170
(i)	With lithium aluminium hydride, synthesis of 2-amino-1-trimethylsilylhexane	170
(ii)	With K-selectride	171
(iii)	With sodium borohydride	171
(iv)	With calcium hydride	172
(v)	By catalytic hydrogenation	172
(vi)	With triphenylphosphine - synthesis of <i>trans</i> -3-butyl-2-trimethylsilylaziridine	173
6.5	Synthesis of trimethylsilylaziridines by the photochemical reaction of alkylazidoformates with vinylsilanes	173
(i)	1-Carboethoxy-2-trimethylsilylaziridine	173
(ii)	<i>Trans</i> -3-butyl-1-carboethoxy-2-trimethylsilylaziridine	174

(iii)	1-Carbomethoxy-2-trimethylsilylaziridine	174
(iv)	1-Carboethoxy-2-(dimethylvinylsilyl)aziridine	175
(v)	Bis(1-carboethoxyaziridin-2-yl)dimethylsilane	176
6.6	Synthesis of vinylsilanes by hydrosilylation of methyl propynoate	176
(i)	Methyl 2-(dimethylphenylsilyl)propenoate	176
(ii)	Methyl 2-(diphenylmethylsilyl)propenoate	177
6.7	General procedure for the synthesis of aziridines by the thermolysis of phenyl azide in the presence of vinylsilanes	178
(i)	2-Carbomethoxy-1-phenyl-2-triethylsilylaziridine	178
(ii)	2-Carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine	179
(iii)	2-Carbomethoxy-2-diphenylmethylsilyl-1-phenylaziridine	179
6.8	The reduction of 1-carboethoxyaziridines	179
(i)	1-Hydroxymethyl-2-trimethylsilylaziridine	179
(ii)	<i>Trans</i> -3-butyl-2-trimethylsilylaziridine	180
6.9	Reaction of <i>trans</i> -3-butyl-1-carboethoxy-2-trimethylsilylaziridine with butyllithium	181
6.10	Ring opening of silylaziridines in CDCl <sub>3</sub> with gaseous hydrogen halides	181
(i)	Ring opening of <i>cis</i> -3-phenyl-2-trimethylsilylaziridine with hydrogen chloride	181
(ii)	Ring opening of <i>trans</i> -3-butyl-2-trimethylsilylaziridine with hydrogen bromide	182
(iii)	Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with hydrogen chloride	182
(iv)	Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with hydrogen bromide	183
(v)	Reaction of 2-carboethoxy-1-phenyl-2-triethylsilylaziridine with hydrogen chloride	183
(vi)	Reaction of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with hydrogen chloride	183
6.11	Reaction of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with 1M hydrogen chloride solution in ether	184
6.12	Ring opening of silylaziridines with trimethylsilyl halides	184
(i)	Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with trimethylsilyl bromide	184
(ii)	Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with trimethylsilyl iodide	185
(iii)	Reaction of 1-carboethoxy-2-trimethylsilylaziridine with trimethylsilyl chloride	185
6.13	Ring opening of silylaziridines with trifluoroacetic acid	186
(i)	Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with trifluoroacetic acid	186
(ii)	Reaction of 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine with trifluoroacetic acid	186
(iii)	Reaction of 1-phenyl-2-trimethylsilylaziridine with trifluoroacetic acid	187
6.14	Ring opening of silylaziridines with trifluoromethanesulphonic acid	187
(i)	Reaction of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with trifluoromethanesulphonic acid	187

(ii)	Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with trifluoromethanesulphonic acid	188
6.15	Reactions of silylaziridines with methyl trifluoromethanesulphonic acid	188
(i)	Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with methyl trifluoromethanesulphonic acid	188
(ii)	Reaction of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with methyl trifluoromethanesulphonic acid	189
6.16	Reaction of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with trimethylsilyl trifluoromethanesulphonic acid	189
6.17	Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with perchloric acid	190
6.18	The reaction of silylaziridines with fluoride ion in the presence or absence of electrophiles	190
(i)	Preparation of 2-carboethoxy-1-phenylaziridine	191
(ii)	Preparation of 2-carboethoxy-2-deutero-1-phenylaziridine	192
(iii)	Fluorodesilylation of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with addition of hexanal	193
(iv)	Fluorodesilylation of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with addition of benzaldehyde	194
6.19	The reaction of silylaziridines with nucleophilic reagents	200
6.19.1	Reaction of silylaziridines with lithium dibutyl cuprate	200
(i)	Reaction of 1-carboethoxy-2-trimethylsilylaziridine with lithium dibutyl cuprate	200
(ii)	Reaction of 1-carboethoxy-2-trimethylsilylaziridine with lithium dibutyl cuprate in the presence of boron trifluoride etherate	200
(iii)	Reaction of <i>cis</i> -3-phenyl-1-propyl-2-trimethylsilylaziridine with lithium dibutyl cuprate	201
(iv)	Reaction of <i>cis</i> -3-phenyl-1-propyl-2-trimethylsilylaziridine with lithium dibutyl cuprate in the presence of boron trifluoride etherate	201
6.19.2	Reactions of silylaziridines with methyl iodide	201
6.19.3	Reactions of 1-carboethoxy-2-trimethylsilylaziridine with amines	201
(i)	Reaction of 1-carboethoxy-2-trimethylsilylaziridine with aniline	201
(ii)	Reaction of 1-carboethoxy-2-trimethylsilylaziridine with aniline in the presence of ethanol	202
(iii)	Reaction of 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine with benzylamine in the presence of alumina	202
(iv)	Reaction of 1-carboethoxy-2-trimethylsilylaziridine with benzylamine in the presence of ethanol	202
6.19.4	Reactions of 1-carboethoxy-2-trimethylsilylaziridine with diethyl malonate anion	202
6.19.5	Reactions of silylaziridines with methyl magnesium iodide	203
(i)	Reactions of 1-carboethoxy-2-trimethylsilylaziridine with methyl magnesium iodide	203
(ii)	Reaction of <i>cis</i> -3-phenyl-1-propyl-2-trimethylsilylaziridine with methyl magnesium iodide	203

## Abstract

A series of new and generally applicable routes to silylaziridines containing a silyl group in the 2-position has been developed with a view to examining the chemical reactivity of such species. Ring opening reactions, ring preserving reactions and fluorodesilylation reactions have been examined in detail. The study also includes an examination of the conjugate addition reactions of some vinylsilanes.

Three new routes to silylaziridines are presented, these are summarized below.

1. The thermal reaction between phenyl azide and functionalized vinylsilanes. This reaction proceeds via an intermediate triazoline and was used to prepare silylaziridines with an *N*-phenyl and an  $\alpha$ -carbomethoxy substituent. Different 2-silyl groups were introduced by this method: triethylsilyl and dimethylphenylsilyl.
2. The lithium aluminium hydride reduction of bromoazides derived from vinylsilanes. This route was used to prepare *N*-unsubstituted aziridines, in some cases stereoselectively. Two methods were employed to prepare the bromoazides, one using an aqueous *N*-bromosuccinimide/sodium azide as an *in situ* bromine azide source, and another using bromine azide generated from bromine and sodium azide in dichloromethane.
3. The photolysis of ethyl or methyl azidoformate in the presence of vinylsilanes. This reaction proceeds via a nitrene intermediate and was used to prepare several substituted silylaziridines.

All of the aziridines were subjected to reactions with electrophilic agents including hydrogen halides, trimethylsilyl halides, trifluoroacetic acid, and the triflates; trifluoromethanesulphonic acid, methyl trifluoromethanesulphonic acid and trimethylsilyl trifluoromethanesulphonic acid with a view to comparing their chemistry from a global perspective. Mainly products of ring opening were observed, however, a richer chemistry is displayed by the more functionalized silylaziridines, i.e., those containing a 1-phenyl and a 2-carboethoxy substituent, where an enamine (trifluoromethanesulphonic acid), an aziridinium salt (trimethylsilyl trifluoromethanesulphonic acid) were produced. Some structure-activity relationships have been drawn.

A study was conducted to find suitable conditions for the fluorodesilylation of silylaziridines. It was found that only silylaziridines that contained activating substituents could be desilylated. Silylaziridines having an *N*-phenyl and an  $\alpha$ -carbomethoxy substituent were active in desilylation reactions, but, only when the silyl group contained a phenyl group (dimethylphenylsilyl) could electrophiles be trapped. Benzaldehyde and

hexanal were active reagents in this respect, however, other aldehydes, or ketones could not be trapped. A mechanism involving the aziridinyll anion and the fluorosilane as a loosely associated ion pair is proposed on the basis of the results obtained.

The study also includes an examination of the conjugate addition reactions of some vinylsilanes.  $\alpha$ -Lithiovinyltrimethylsilane reacts with ethyl chloroformate, ethyl acetate, acetic anhydride and dimethylcarbonyl chloride to produce  $\alpha,\beta$ -unsaturated carbonyl compounds which act as Michael acceptors to the starting material,  $\alpha$ -lithiovinyltrimethylsilane. The fate of the resultant enolate is dependant on the properties of the enolate and the electrophile.

## CHAPTER 1

---

### INTRODUCTION

#### 1.1 Introduction to organosilicon chemistry

##### 1.1.1 Preliminary considerations

The introduction of silicon to organic chemistry came in 1865 when Friedel and Crafts<sup>1</sup> reported the synthesis of the first organosilicon compound, tetraethylsilane from diethyl zinc and silicon tetrachloride. Subsequently, from 1898 to 1939 Frederick Kipping carried out the first systematic studies on organosilanes at the University of Nottingham.

With the greater commercial availability of silicon containing reagents in the last twenty five years, research in the area of organosilicon chemistry has accelerated and the value of silicon as a synthetic tool has been more widely recognised.

The value to the synthetic chemist of organic compounds containing silicon is related to the unusual bonding properties which they exhibit. In brief, the effects which dominate organosilicon chemistry stem from relative bond strengths, relative electronegativities, as well as the influence from silicon d-orbitals. As a consequence of these combined effects, silicon may be described as a mild metal (or like a large proton) and therefore a highly versatile element.

##### 1.1.2 Physical properties of organosilanes

Electronegativity data<sup>2</sup> indicate that silicon is much more electropositive than carbon. Average bond energy data<sup>3</sup> show that silicon forms strong bonds with fluorine, oxygen, nitrogen, chlorine and other electronegative elements. Those two statements summarize much of the chemistry of silicon. The low electronegativity of silicon compared with

carbon means that the carbon-silicon bond is polarized<sup>4</sup>  $\text{Si}^{\delta+}\text{C}^{\delta-}$  resulting in a tendency for bond cleavage in the direction  $\text{Si}^+\text{C}^-$ . Thus, silicon bonded to carbon is susceptible to nucleophilic attack and undergoes bimolecular nucleophilic substitution with ease, especially when the nucleophile is an alkoxide, fluoride or chloride ion. While homolytic fission would be expected to be faster than for the corresponding carbon analogue, unimolecular substitution is not observed partly because of the speed of the  $\text{S}_{\text{N}}2$  reaction.

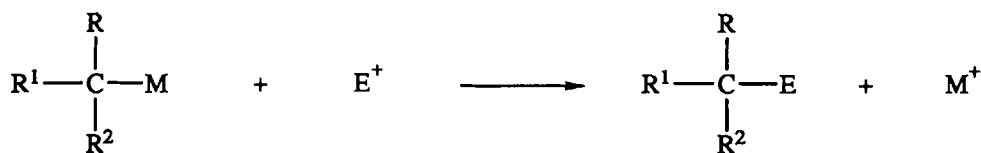
High silicon-fluorine and silicon-oxygen bond energies introduce the possibility of fluoride or alkoxide ion mediated desilylation which is highly useful and has been accomplished (this area will be discussed in detail in Chapter 4). However the high silicon-oxygen bond strength makes silyl compounds susceptible to hydrolysis and this necessitates that some silyl compounds be handled in a dry atmosphere.

While polarization of the carbon silicon bond is important, it is less significant when compared with that in other organometallic reagents in which the ionic character of the carbon-metal bond is much greater. This is illustrated in the Pauling electronegativity values given in Table 1.1.

**Table 1.1** Percentage ionic character of carbon-metal bonds according to Pauling electronegativities

Metal	K	Na	Li	Mg	Zn	Cd	Si	H
% Ionic character	51	47	43	35	18	15	12	4

This means that while organometallic reagents undergo electrophilic substitution (Equation 1.1), reactivity declines in the series Li, Mg, Zn, Cd as the polarization of the  $\sigma$ -bond decreases so that silyl compounds are relatively unreactive towards electrophiles.



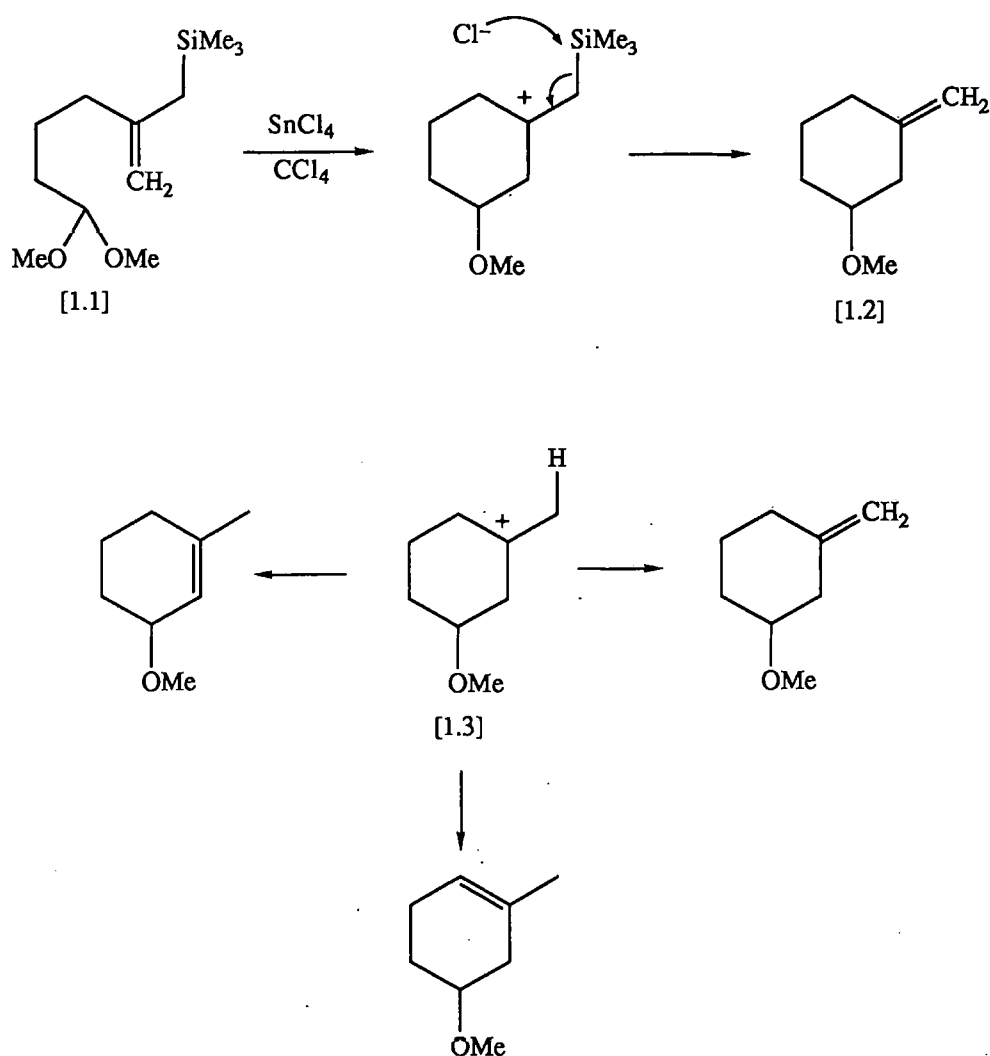
Equation 1.1

This confers an advantage on silicon over other metals in organic synthesis in that they can generally be handled more easily. Normally they do not require rigorously anhydrous or inert atmospheres and are inert in the presence of most functional groups. In consequence, it is often possible to carry out reactions elsewhere in the molecule without affecting the carbon-silicon bond.

When carbon-silicon bond cleavage does occur, it is always in the direction  $\text{Si}^+\text{C}^-$  i.e., in the same direction that carbon-hydrogen bonds are cleaved. It is therefore often possible to predict the behaviour of a carbon-silicon bond by analogy with the corresponding situation with a carbon-hydrogen bond. Moreover, the extent of polarization in the carbon-silicon bond is greater than in the carbon-hydrogen bond and so generally, organosilicon compounds are more reactive than the corresponding hydrocarbons.

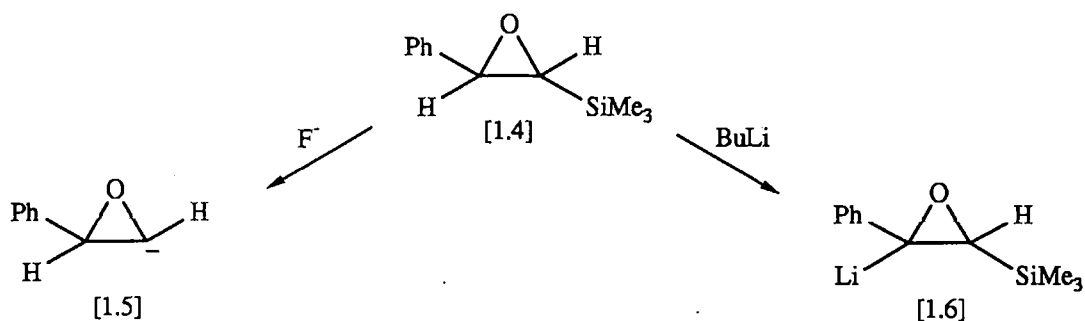
In a situation where competition is possible, a carbon-silicon bond is more reactive towards oxygen and halogen nucleophiles or bases, whereas a carbon-hydrogen bond is the more reactive towards carbon and nitrogen nucleophiles or bases<sup>5</sup>. This phenomenon is illustrated by the examples given in Schemes 1.1 and 1.2. In the first example, the directive influence of the silicon moiety in [1.1] leads to just one alkene, [1.2], but when silicon is replaced by hydrogen, as in [1.3], three sites for proton abstraction are possible and do occur.





Scheme 1.1

Analogously in the following example (Scheme 1.2), fluoride ion attacks at the silicon atom of the epoxystyrene [1.4], leading to the desilylated product [1.5], whereas the carbon nucleophile preferentially abstracts the acidic benzylic proton to give [1.6].

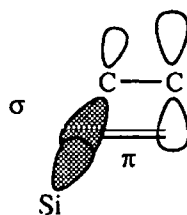


Scheme 1.2

### 1.1.3 Directive effects of the silyl group

Silicon unlike carbon possesses low lying vacant 3d orbitals. The availability of these low lying empty orbitals contribute both to the reactivity of organosilicon compounds and towards directing the stereochemical outcome.

Anions  $\alpha$ - and carbonium ions  $\beta$ - to silicon exhibit enhanced stability. The ability of a silyl group to promote the development or formation of a carbonium ion species in the  $\beta$ -position is known as the ' $\beta$ -effect'<sup>7</sup> and its interpretation constitutes a matter of some controversy. It has been proposed that stabilization is achieved through a bridging mechanism<sup>8,9</sup> but perhaps the most widely accepted explanation concerns hyperconjugative stabilization<sup>10,11</sup>. In this case, stabilization is achieved through  $(p-\sigma)\pi$  conjugation between the carbon-silicon bond and the developing positive charge in the transition state for reaction.



This  $(p-\sigma)\pi$  conjugation may play a role in weakening the carbon-silicon bond and thus promote the cleavage process.

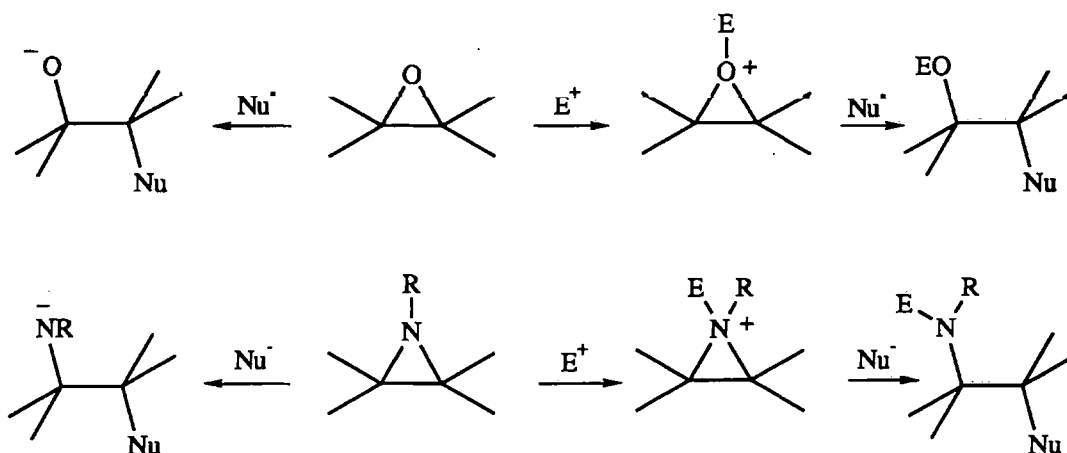
## 1.2 The synthetic utility of 2-silylated heterocycles

### 1.2.1 Some chemistry of 3-membered heterocycles

The range of synthetic opportunities open to such simple molecules as aziridines or epoxides is immediately widened by the introduction of a silicon containing group. In such compounds, silicon's value as a synthetic reagent is manifested not only in its ability to

activate the molecule towards attack, but also in its directive influence. Thus the introduction of functionality can be mediated in a stereo-controlled manner.

Three membered heterocycles such as epoxides or aziridines are important intermediates in organic synthesis for several reasons. Their chemistry is dominated by the ring strain that confers enhanced reactivity. The ring systems are attacked by a variety of reagents. This may be by direct nucleophilic attack and or by initial electrophile coordination with the heteroatom (Scheme 1.3).



Scheme 1.3

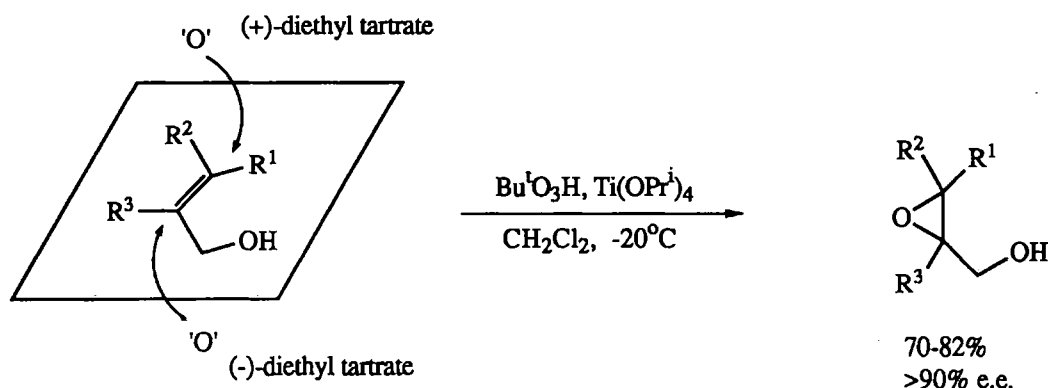
Thus ring opening can lead to a wide variety of useful products.

Although the influence of silicon can assist the asymmetric synthesis of aziridines and epoxides, the ability of the silicon moiety to direct regio and stereochemistry is of great importance. Non-silylated aziridines and epoxides undergo nucleophilic ring cleavage predominantly at the less substituted<sup>12</sup> carbon atom of the ring unless one of them has dialkyl or benzyl substitution. When the epoxide or aziridine, contains a silyl species in the 2-position, with few exceptions, a nucleophile will attack the carbon  $\alpha$ - to the silicon atom. This is due to the directing effect of the silicon moiety and this is described in section 1.2.3. A detailed comparison of ring opening reactions of silyl substituted and non-silyl substituted aziridines is given in Chapter 3 of this thesis.

### 1.2.2 Introduction to the chemistry of silylepoxides

Silylepoxides have received considerable attention in the chemical literature as synthetic intermediates<sup>13,14</sup>. The methods available for ring synthesis of the epoxides are limited largely to the oxidation of vinylsilanes<sup>15</sup> and more recently<sup>16</sup>, the condensation of  $\alpha$ -chloromethyl alkyl/aryl silyl anions with carbonyl compounds. The route from vinylsilanes is of particular importance as both the regio and stereochemical features of the parent vinylsilane are retained on epoxidation, so highly stereoselective syntheses are possible.

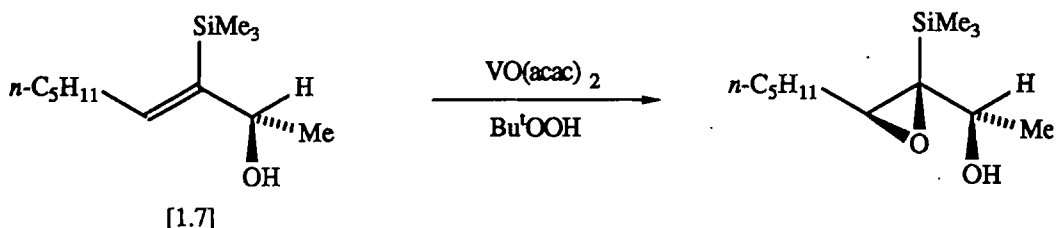
While general peroxidation methods<sup>17</sup> will lead to pure *cis* or *trans* epoxides, the final product mixture is always racemic and chiral separations are often difficult or impossible. Sharpless<sup>18-20</sup> has devised the first practical method for asymmetric epoxidation. With allylic alcohols, in the presence of either (+)-diethyl tartrate or (-)-diethyl tartrate, oxygen is delivered from one enantioface to yield a single epoxide with greater than 90% enantiomeric excess (Scheme 1.4).



Scheme 1.4

Other researchers have subsequently investigated other asymmetric epoxidation routes. Tomioka and co-workers<sup>21</sup> have shown that the epoxidation of chiral allylic alcohols carrying a trimethylsilyl group on the double bonds, e.g., [1.7] in Equation 1.2, with

VO(acac)<sub>2</sub>Bu<sup>t</sup>OOH or *meta*-chloroperbenzoic acid provides *erythro* or *threo* epoxy alcohols respectively with high stereoselectivity. Generally, the greatest selectivity was observed with the vanadium reagent where diastereoisomeric ratios were of the order of 99:1.



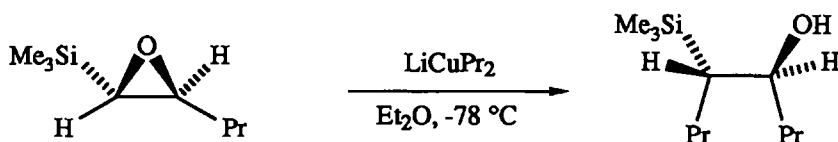
Equation 1.2

The observed selectivity could be explained in terms of the steric bulk of the trimethylsilyl group. Interestingly, the silyl group could easily be removed with fluoride ion, subsequent to epoxidation. This could be achieved using either cesium fluoride or tetrabutylammonium fluoride and full retention of configuration at the oxiranyl carbon was observed. Successful desilylation of silylaziridines was a major goal of this thesis and as such, the subject has been discussed in some depth in Chapter 4.

Unlike the nitrogen analogs, silylepoxide chemistry is well known. The reactions that have been carried out with silylepoxides range from electrophilic and nucleophilic ring opening to deprotonation and also desilylation. Thus, silylepoxides provide a starting point in a wide variety of useful and often stereospecific syntheses.

### 1.2.3 Reactions of silylepoxides involving ring cleavage

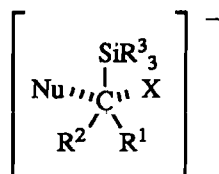
When treated with nucleophiles, silylepoxides undergo ring opening. These reactions are useful because they proceed in a stereo and regiospecific manner as in the example illustrated in Equation 1.3.



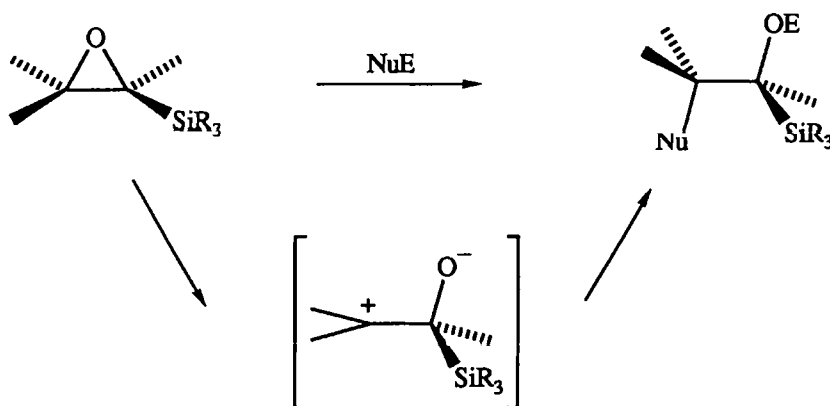
Equation 1.3

Whether by direct nucleophilic attack or by initial association of electrophiles on the ring oxygen atom,  $\alpha$ -opening occurs<sup>14,22-27</sup>.

Bond cleavage  $\alpha$  to silicon may appear to be the more unlikely mode, in view of the well known stability of carbonium ions  $\beta$  to silicon, combined with the evidence for silicon's destabilizing effect on  $\alpha$ -carbonium ions. This regiochemistry may be rationalised when we consider that silicon can stabilize the incipient negative charge development on the  $\alpha$ -carbon in the transition state for substitution. This may occur in nucleophilic substitution reactions where substantial nucleophile-carbon bond formation precedes carbon-leaving group bond cleavage.



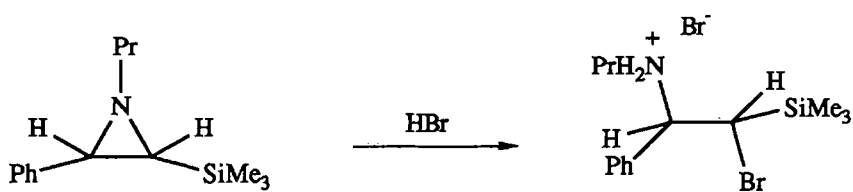
If the  $\beta$ -effect were playing a dominant role then an  $\text{S}_{\text{N}}1$  pathway would be preferred leading to  $\beta$ -cleavage as in Scheme 1.5.



Scheme 1.5

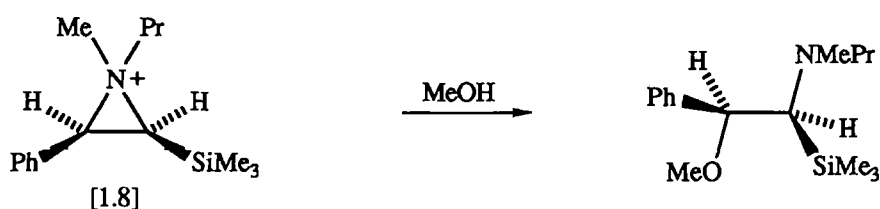
The intermediate would be a  $\beta$ -carbonium ion which one might expect to be stabilized by hyperconjugation or  $\pi$ -(p-d) $\pi$  bonding. However, hyperconjugative stabilization is only very weak as the carbon p-orbital containing the developing charge and the carbon-silicon bond are unable to obtain a coplanar geometry<sup>28</sup>. Thus unless stronger directing effects dictate otherwise, silylepoxydes undergo  $\alpha$ -C-O cleavage whether ring opening is nucleophilic or electrophilically assisted.

Similarly, 2-silylaziridines also undergo  $\alpha$ -ring opening as has been recently demonstrated by Soobramanien<sup>29</sup> the only worker to publish results on ring opening reactions of silylaziridines to date. An example is given in Equation 1.4.



Equation 1.4

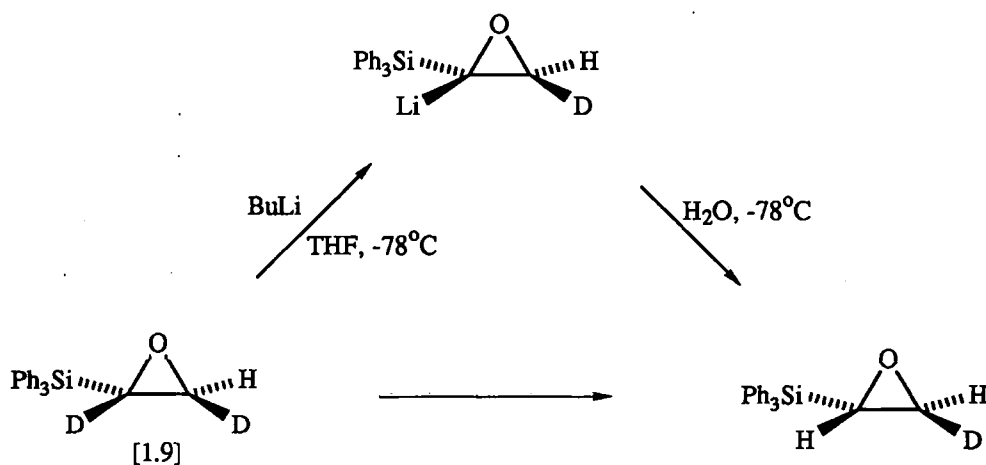
However with the quaternary aziridinium salt, [1.8] shown in Equation 1.5, an  $S_N1$  like mechanism prevails because the resonance stabilization by the phenyl group becomes more important.  $\beta$ -C-N cleavage occurs ahead of O-C bond formation in the transition state which thus has considerable  $sp^2$  character. This example is the only known exception to the general rule of attack at the  $\alpha$ -carbon.



Equation 1.5

#### 1.2.4 $\alpha$ -Deprotonation-metalation of silylepoxides

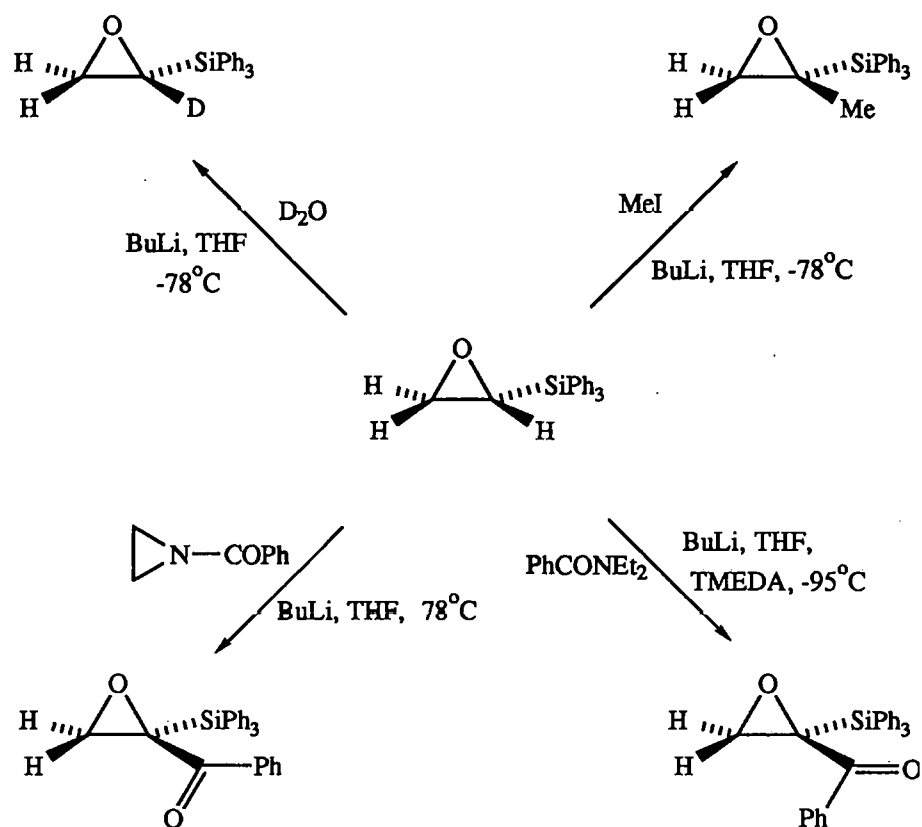
Since anions  $\alpha$ - to silicon are especially stable species one might imagine a proton in the  $\alpha$ -position to be sufficiently acidic to be removed with strong bases such as butyllithium. Indeed, Eisch and Galle<sup>6,30,31</sup> have shown that it is possible to deprotonate and metalate a range of silylepoxides in the  $\alpha$ -position. That these lithiations occur with retention of configuration and retain their stereostructural integrity at low temperature, was demonstrated by the lithiation of a *cis*-dideuterioepoxysilane<sup>31</sup>, [1.9], Scheme 1.6.



Scheme 1.6

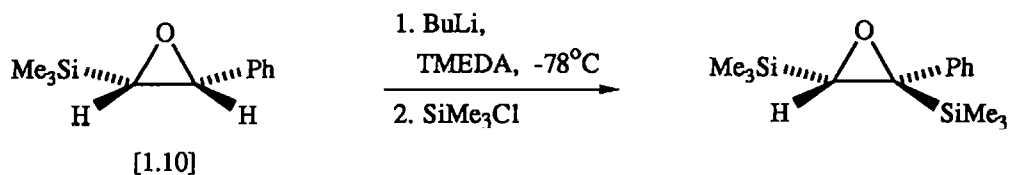
This finding was of great consequence, as such an intermediate could be a precursor to carbonyl, hydroxy, alkyl etc., functions as well as a unit bearing two adjacent carbon centres of defined chirality. Various quenching agents have been used in these reactions, giving a range of end products substituted in the  $\alpha$ -position (Scheme 1.7).



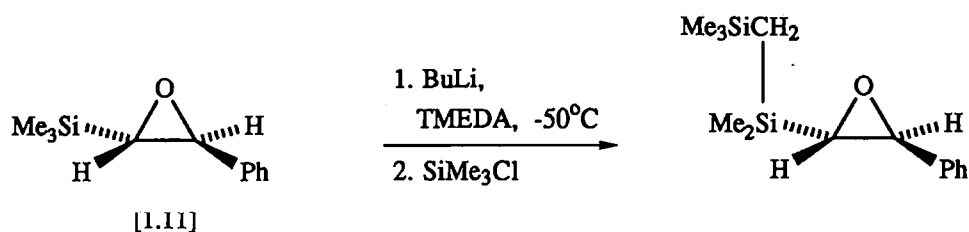


Scheme 1.7

However, when the epoxide had a  $\beta$ -phenyl substituent in a *cis* conformation (as in [1.10], Equation 1.6), lithiation took place  $\alpha$  to the phenyl group, whereas when the phenyl group was in the *trans* position ([1.11], Equation 1.7), a proton is abstracted from one of the methyl protons in the trimethylsilyl group itself.

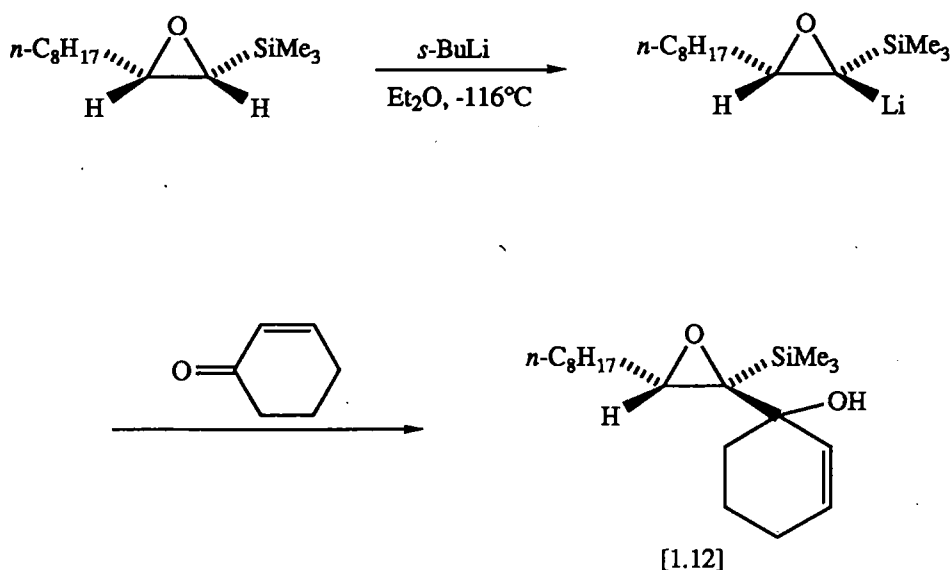


Equation 1.6



Equation 1.7

Molander<sup>32</sup> has also investigated the  $\alpha$ -metalation reactions of silylepoxides. Moreover, he has shown that certain electrophilic trapping reactions, in particular those involving ketones or conjugated aldehydes, proceed with excellent diastereoselectivity. In the following example, (Scheme 1.8) the product alcohol, [1.12], was obtained with 98.6% diastereoselectivity.



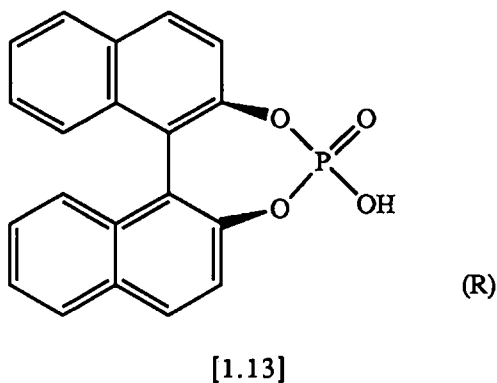
Scheme 1.8

### 1.2.5 2-Trimethylsilylaziridines as synthetic intermediates

While few general syntheses of epoxides are available, aziridines may be made by a number of routes. However, these are largely inaccessible using silyl reagents and little to date has been reported on the synthesis of C-silylaziridines, and even less on the reactivity of these compounds. Such syntheses would be extremely desirable as aziridines are open

to a wider selection of synthetic manipulations than are epoxides. In addition, aziridines may be quaternized and the salts formed from silylated aziridines are often stable and easily isolated. The non-silyl counterparts however do not in general form appreciably stable salts.

The ability to quaternize aziridines is important for several reasons. The introduction of functionalization at the nitrogen becomes possible and the resultant salt is activated towards attack by nucleophiles. Also, the positive charge on nitrogen would render a hydrogen atom  $\alpha$  to silicon especially acidic compared with the neutral aziridine. This is due to the formation of a zwitterionic intermediate which would contain both an  $\alpha$ -anionic and a  $\beta$ -carbocationic site and such a species would be expected to be especially stable. Whilst Eisch and Galle<sup>6,30,31</sup> have successfully deprotonated and metalated silyl epoxides, no attempts to reproduce these results in silylaziridines has been reported in the literature to date. A further advantage of the stability of quaternary aziridinium salts lies in the possibility of resolving a racemic mixture of aziridines via a chiral acid.



A suitable acid which has been used for this purpose in the past<sup>29</sup> is (R)-(-)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate, [1.13].

The two chiral aziridinium salts thus formed can be fractionally crystallized with optical rotation monitoring, until optically pure samples are obtained. Although expensive, the acid may be recovered by treatment with a more basic amine and reused.

### 1.3 Synthesis of 2-silylaziridines

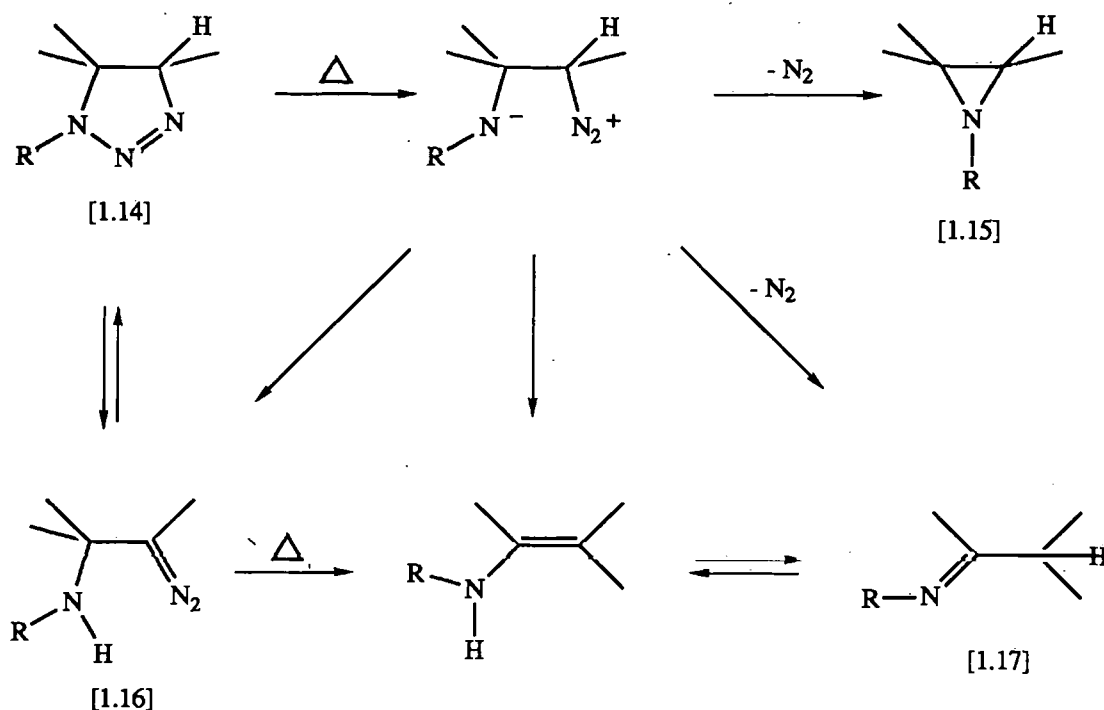
#### 1.3.1 Syntheses of silylaziridines by the reaction of arylazides with vinylsilanes

Although silylepoxides have received much attention in the chemical literature, little has been reported on aziridines containing a carbon-silicon bond.

The first silicon containing aziridine was synthesized in 1964 by Adrianov and Sidorov<sup>33,34</sup> who obtained silylated aziridines through the thermal reactions of aryl azides with vinylsilanes. The reaction of aryl azides with alkenes is a popular method of aziridine synthesis and has provided a route to 2-silylaziridines for several workers as will be discussed in this Chapter.

The dipolar character of the azido group<sup>35</sup> is such that it is able to undergo 1,3-dipolar cycloaddition reactions with olefins forming 1,2,3-triazolines. Kinetic studies show that the reaction of alkenes with organic azides are concerted, stereospecific, *cis* additions<sup>36,37</sup> and the geometry of the alkene is retained in the triazoline adducts<sup>38</sup>. The direction of addition is controlled by electronic rather than steric factors<sup>39</sup>, the terminal nitrogen atom of the azido group binding to the more nucleophilic carbon of the olefin. Unsymmetrically substituted alkenes, unlike acetylenes, yield only one triazoline isomer, as in the case of the reaction of styrene and phenyl azide where the 1,5-diaryltriazoline is formed exclusively<sup>40</sup>. *para*-Nitrophenyl azide is an exception however. When the alkene possesses an electron withdrawing group, this group appears in the product at the 5 position, whereas electron releasing substituents end up at the 4 position. Electron rich azides add particularly easily to electron poor alkenes and vice versa<sup>41</sup>. Triazolines may yield aziridines with extrusion of nitrogen by thermal or photochemical means. The thermal stability of a triazoline is determined largely by electronic factors. The more electron withdrawing the substituent on nitrogen, the greater the ease with which the triazoline is thermally decomposed. The influence of substituents on the ring carbons is less well known. However, electron withdrawing groups on C-4 in the triazoline lead mainly to the aziridine on thermolysis

with a marked retention of triazoline geometry, whereas aziridines are seldom obtained from triazolines having an electron withdrawing group at the C-5 position. For a thermal reaction, imines or the isomeric enamines<sup>42</sup> may also be produced in addition to, or at the expense of the aziridine. The thermolysis of ring opened diazo compounds [1.16] derived from isomerization of triazolines of the type [1.14], leads to enamines, [1.17], whereas direct thermolysis of the triazoline leads to aziridines, [1.15] (Scheme 1.9).



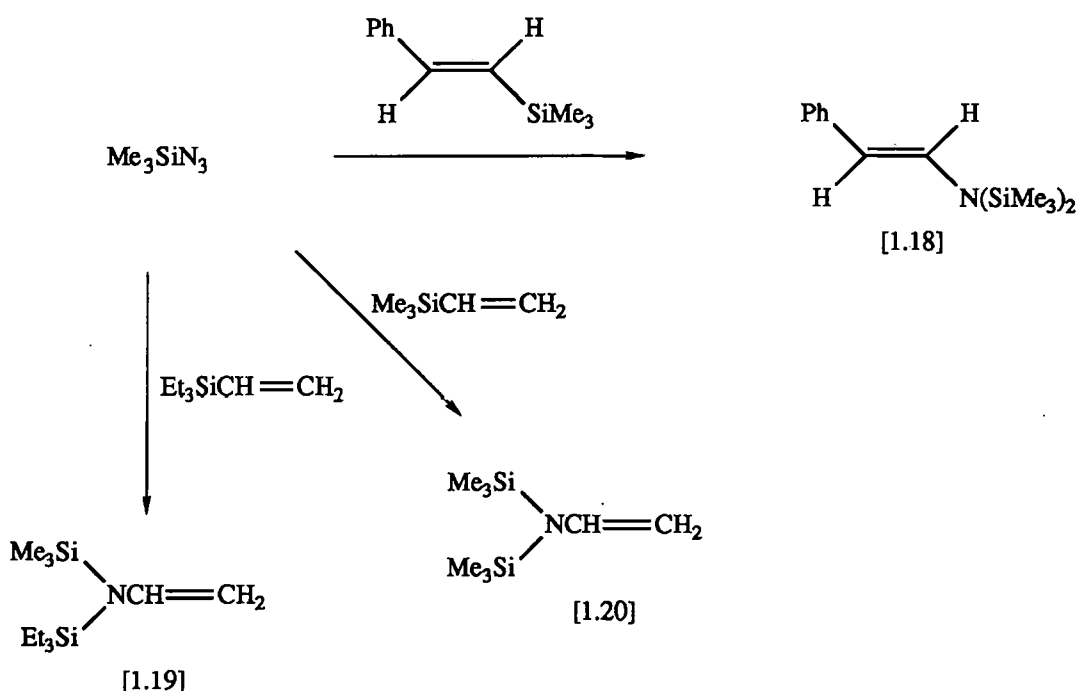
**Scheme 1.9**

When the rate of triazoline/diazo compound isomerization is slow, a high percentage of the aziridine is favoured. However, when a significant amount of the ring opened isomer is present, the enamine is the major product. In situations where the isomerization reaction is spontaneous, higher reaction temperatures favour aziridine formation as direct thermolysis becomes faster than the isomerization<sup>43</sup>.

The photochemical route ( $\lambda > 240$  nm) is more selective than the thermal route yielding the aziridine as the major product. The photolytic reaction is essentially independent of substituent and solvent effects. In some cases imines are obtained in addition to the

aziridine product<sup>44</sup>. Although the reaction is not in general stereospecific, a predominance of retention of configuration is observed.

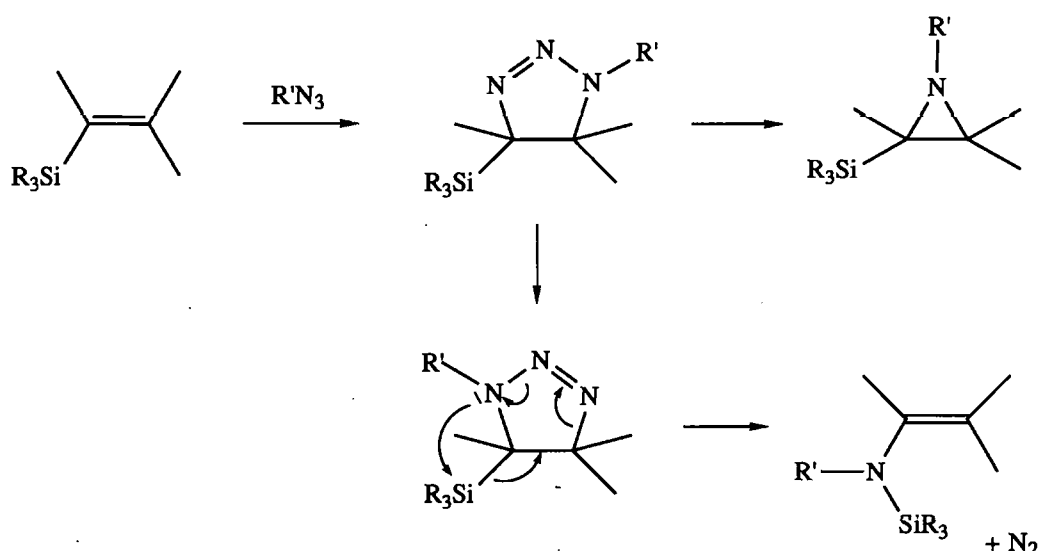
Subsequent to the work of Adrianov and Sidorov<sup>33,34</sup>, Ettenhuber and Ruhlmann claimed that *N*-silylated aziridines could be made by reacting vinylsilanes with trimethylsilyl azides. However, ten years later in 1978 Bassindale and co-workers<sup>45</sup> reinvestigated their findings. They found that by heating trimethylsilyl azide with *trans* trimethylsilylstyrene, vinyltriethylsilane or vinyltrimethylsilane under various conditions they obtained the corresponding bis(silyl)enamines, [1.18], [1.19] and [1.20].



Scheme 1.10

These enamine products are expected to have resulted from the thermal rearrangement of an intermediate triazoline (Scheme 1.11). However, no intermediate cycloaddition product could be detected when the reaction was monitored by NMR spectroscopy. In the same publication, results of a study in which *para*-bromophenyl azide was heated with vinyltrimethylsilane or *trans*-trimethylsilylstyrene were also reported. Their findings support those of Adrianov and also threw new light on the possible mechanism. In this

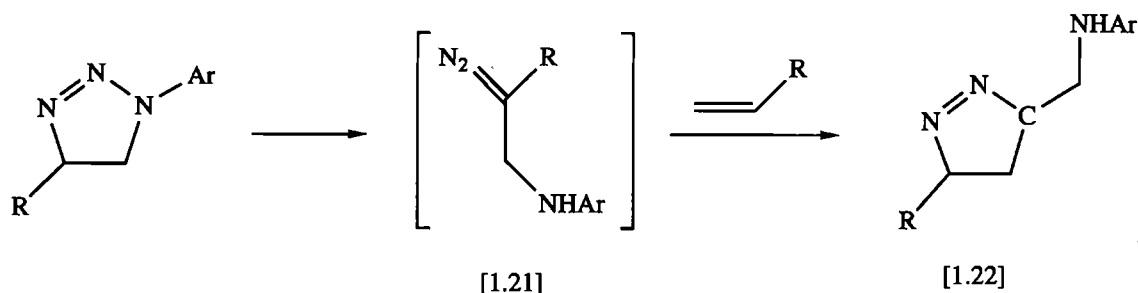
latter case the intermediacy of triazolines was detected by NMR spectroscopy and their conversion to aziridines was monitored. As well as the expected aziridines a small amount of a silylenamine was also detected. Since the aziridines themselves showed no evidence of rearrangement to silylenamines, it was concluded that the silylenamines (and the bis(silyl)enamines) had arisen from a rearranged triazoline. The possibility of a mechanism involving an intermediate diazo compound was not discussed.



Scheme 1.11

Zanirato<sup>46</sup> also, has described the synthesis of silylaziridines using the thermal reaction between aryl and heteroaryl azides with vinylsilanes. In this case, intermediate triazolines were isolated in almost pure form. These were identified, and stereostructural designations assigned on the basis of NMR spectroscopic data. Silylaziridines were obtained from the thermal reaction of vinyltrimethylsilane with a selection of azides including; phenyl, *para*-nitrophenyl, *para*-methoxyphenyl, *para*-chlorophenyl azides and 2- or 3-azidobenzo[b]thiophene. These reacted at room temperature to generate the corresponding 1-substituted, 4-silylated-1,2,3-triazolines. The thermal behaviour of the triazolines was found to be strongly dependent on the activating or deactivating effects imposed by the N-1 substituents. No imine or enamine products were observed, as had been the case in a

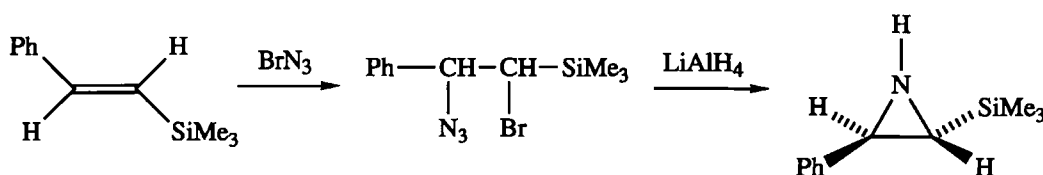
previous study. However, the intermediacy of a diazo compound, [1.21] was suggested by the product obtained, [1.22], when an excess of vinylsilane was present (Scheme 1.12).



Scheme 1.12

### 1.3.2 Syntheses of silylaziridines by the reduction of silylhaloazides

Duboudin<sup>47</sup> described a route to silylaziridines via the reduction of silylhaloazides derived from silylalkenes (Scheme 1.13). It was claimed by Duboudin that the bromoazide prepared from *trans*-trimethylsilylstyrene on reduction with lithium aluminium hydride yields the *trans* aziridine (along with an unidentified olefinic species).



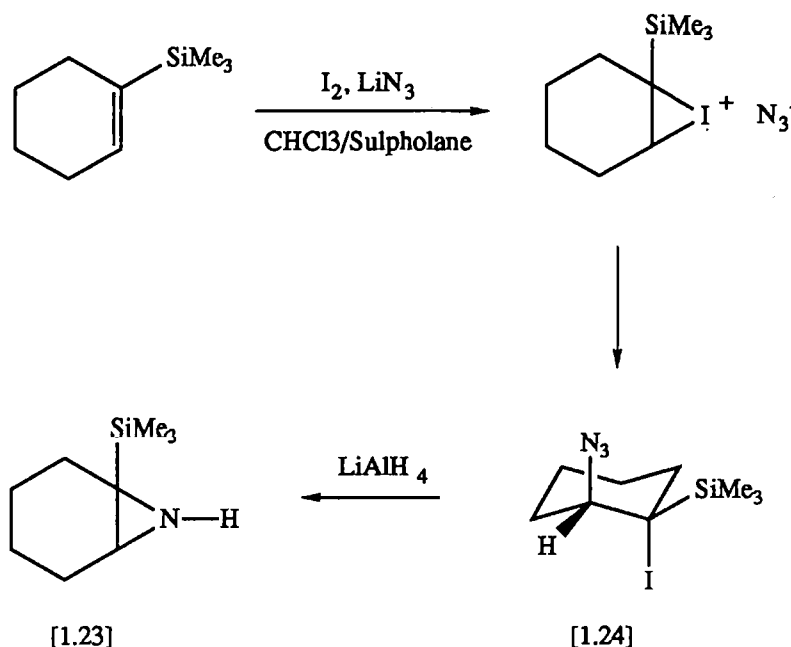
Scheme 1.13

In the current work using the same starting alkene, we have been able to isolate two bromoazides with the same regiochemistry as encountered by Duboudin, but having different diastereoisomeric designations depending on the method chosen. These could be reduced either to the *cis* or the *trans* aziridine in good yield by lithium aluminium hydride reduction, as will be described in a later Chapter.



Duboudin<sup>48</sup> had also made the same aziridine by reduction of the corresponding iodoazide. In this case, two isomerically different azides were identified, present in a ratio of 9:1. A small amount of the RS/SR compound had resulted from some *cis*-trimethylsilylstyrene which was present in the starting material. This on reduction gave a small amount of the *cis*-aziridine which was identified using NMR coupling constants.

Thomas and Whitham<sup>49</sup> also report the synthesis of a silylaziridine, [1.23] by reduction of an iodoazide adduct, [1.24], obtained from 1-trimethylsilylcyclohexene (Scheme 1.14).



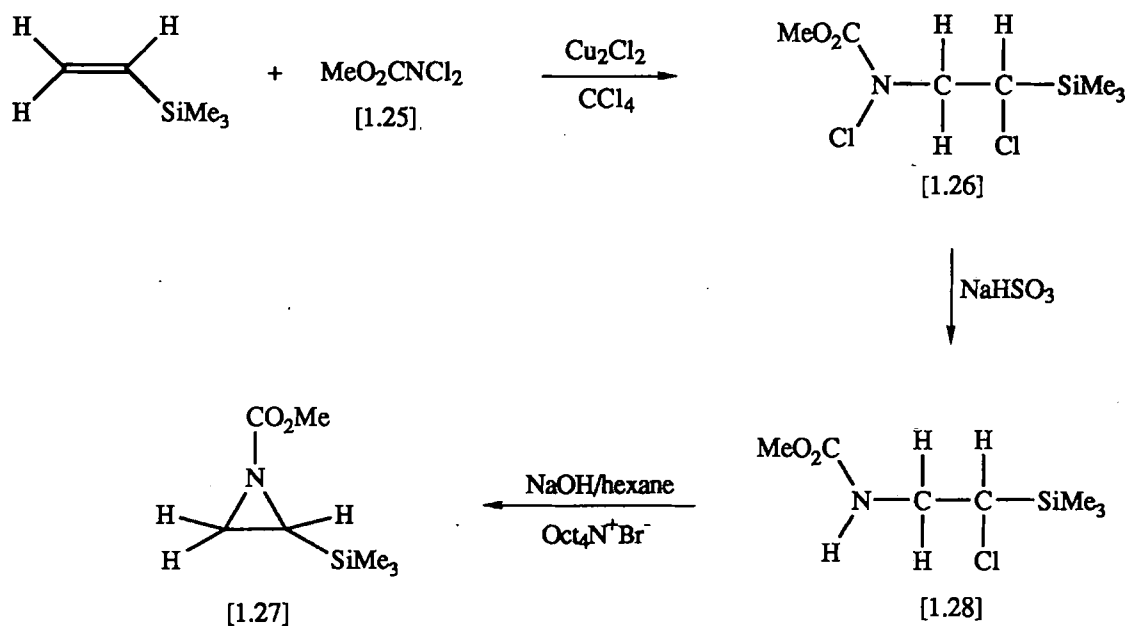
Scheme 1.14

Whitham interpreted the high degree of regio and stereoselectivity, observed in the formation of the iodo azide adducts, in terms of an intermediate iodonium ion. This undergoes nucleophilic attack by azide ion (diaxial opening), at the carbon atom β to the silyl group. This orientation is in contrast to the normal mode of opening postulated for the ring opening of silyl epoxides, which without known exceptions occurs α to the silyl group. Whitham suggests that the transition state for the iodonium ion opening has a relatively high carbonium ion character and is stabilized by the β-silyl group. The same

authors later reported<sup>50</sup> a more detailed investigation of the regio and stereochemical aspects of the addition of iodine based electrophilic reagents to vinylsilanes. They make a comparison with the mode of ring opening of the corresponding silylepoxides and conclude that the reaction is unlikely to be controlled by the steric effect of the silyl group - the greatest influence being the stabilizing effect of the silyl group on an S<sub>N</sub>1-like transition state. This area will be discussed in more detail in Chapter 2.

### 1.3.3 Syntheses of silylaziridines by cyclization of silylated chlorocarbamates

A silicon-containing aziridine with an *N*-carbomethoxy substituent was prepared in 1984 by Lukevics and co-workers<sup>51</sup> but by a rather lengthy procedure (Scheme 1.15).



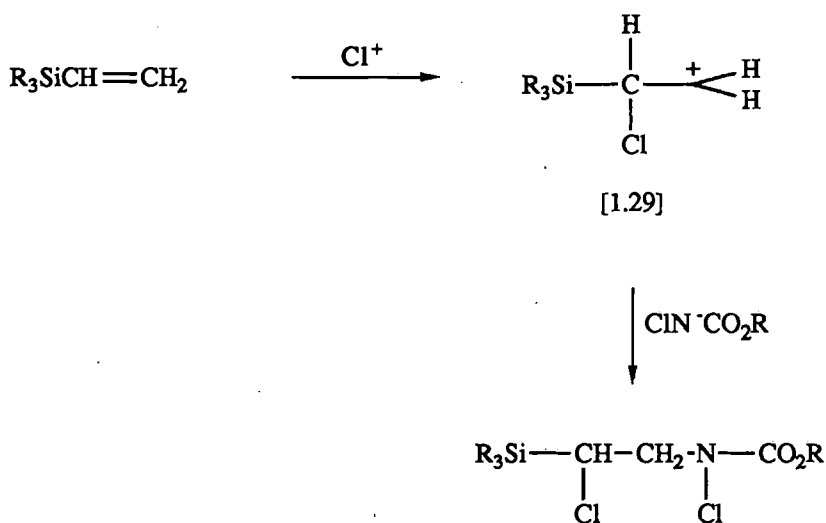
Scheme 1.15

Pseudohalogens such as dialkyl dichlorocarbamates and *N,N*-dichloroarenesulphonamides have previously been shown to form adducts with alkenes<sup>52</sup>. Lukevics used this reaction as a starting point for his synthesis (Scheme 1.15). Addition of methyl *N,N*-dichlorocarbamate, [1.25] to vinyltrimethylsilane leads to the formation of a silylated

carbamate, [1.26]. Subsequent reduction of [1.26] with sodium hydrogen sulphite yielded methyl *N*-(2-chloro-2-trimethylsilyl)ethyl carbamate [1.28]. Phase transfer catalytic assistance (ultrasonic irradiation) in hexane with solid sodium hydroxide facilitated intramolecular alkylation to give 1-carbomethoxy-2-trimethylsilylaziridine [1.27].

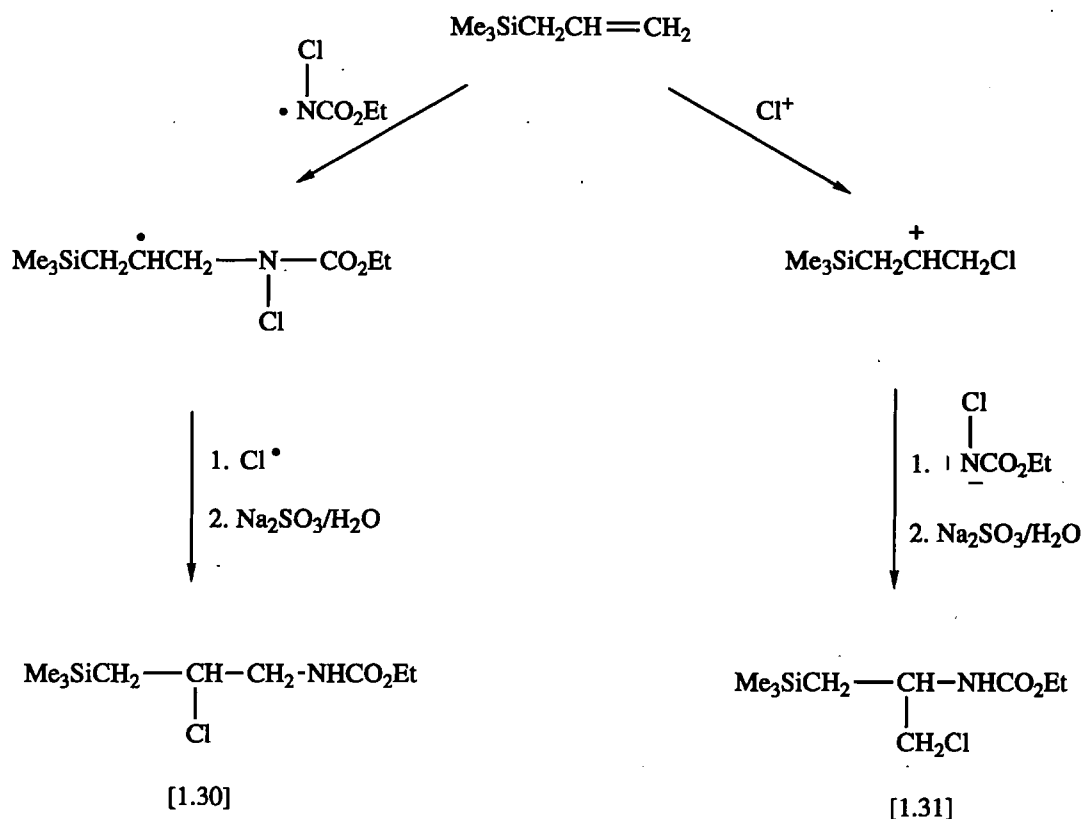
An interesting feature of this synthesis is that the orientation of addition of alkyl dichlorocarbamate, [1.25] in the first step is always anti-Markownikov whether an ionic or radical reaction occurs. Previous studies<sup>53,54</sup> showed that the orientation of adduct formation was dependant on whether a radical or ionic pathway is followed.

Dichlorocarbamates react with vinylsilanes in air in the absence of a catalyst suggesting an ionic mechanism. An explanation for the observed regiochemistry of addition lies in the ability of silicon to stabilize an intermediate  $\beta$ -carbonium ion such as [1.29] in Scheme 1.16.



Scheme 1.16

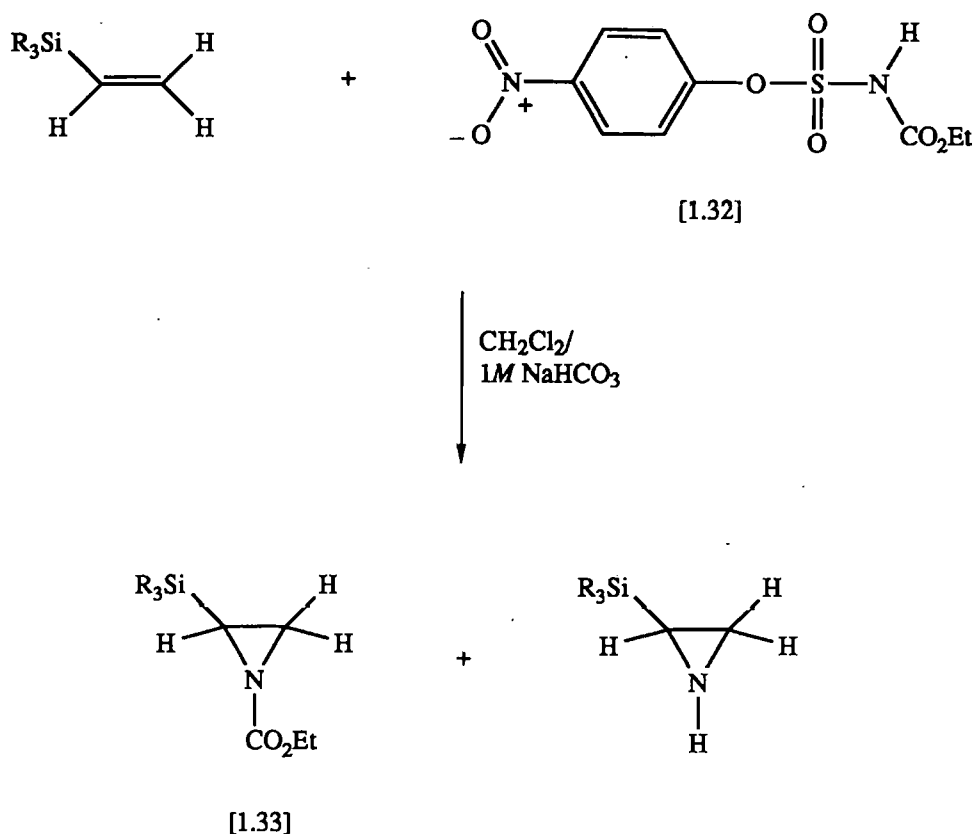
The reaction of allyltrimethylsilane and alkyl dichlorocarbamates however is not stereospecific.



Scheme 1.17

In the above reaction Scheme, (where  $\text{Cu}_2\text{Cl}_2$  was used as a radical initiator) the two possible regioisomers, [1.30] and [1.31], of the silicon containing carbamate are generated in a 1:1 ratio. This may be due to attack by either  $\text{Cl}^+$  or  $\bullet\text{N}(\text{Cl})\text{CO}_2\text{Et}$ . Both of these products, on cyclization led to an aziridine with the trimethylsilyl group separated from the ring by a methylene group. As such, it was the first silyl compound of its type to be isolated.

In a later publication<sup>55</sup> Lukevics studied a new route to 1-carboethoxy-2-trimethylsilylaziridine [1.33]. Ethoxycarbonylnitrene, which may be generated by a photolytic<sup>56</sup> or an  $\alpha$ -elimination<sup>57,58</sup> route has long been known to react with alkenes yielding *N*-carboethoxyaziridines<sup>56-59</sup>. Lukevics has carried out such a reaction under liquid phase transfer catalysis, the nitrene intermediate being generated by base induced  $\alpha$ -elimination of *para*-nitrobenzenesulphonate anion, [1.32] from *N*-(*para*-nitrobenzenesulphonyloxy) carbamate.



Scheme 1.18

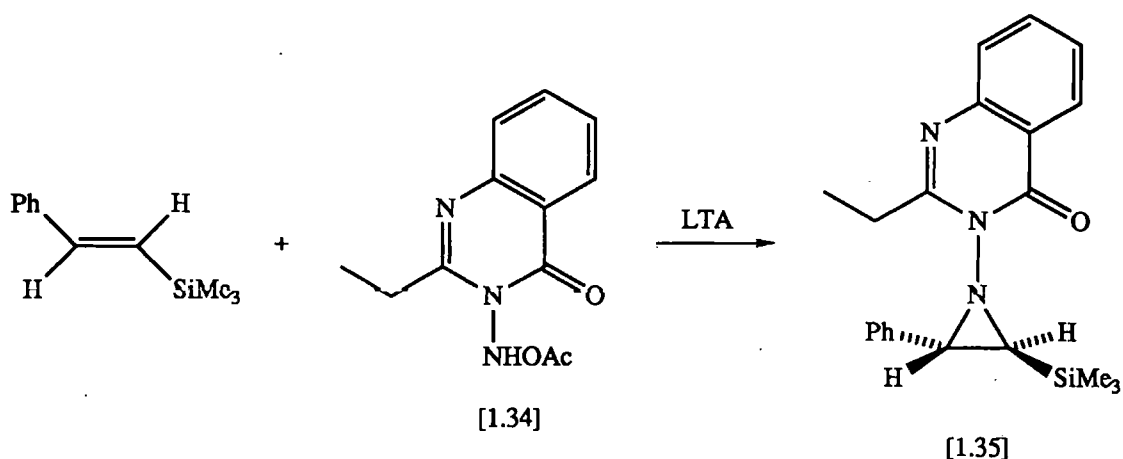
A much cleaner and more facile general synthesis of such aziridines has been developed in the current work, where the nitrene intermediate was produced by the photochemical decomposition of ethyl azidoformate in the presence of neat vinylsilanes. With vinyltrimethylsilane, 1-carboethoxy-2-trimethylsilylaziridine, [1.33] was generated as the sole product. The method has been extended to give aziridines using other vinylsilanes and another alkyl azidoformate.

#### 1.3.4 Syntheses of silylaziridines by the reaction of a quinazolone nitrene with vinylsilanes

The formation of aziridines by the reaction of alkenes with nitrenes seldom occurs in good yield. However, Atkinson has developed a method for such a synthesis which is not only high yielding, but also displays a significant amount of chiral induction<sup>60,61</sup>. One of the

compounds used to generate nitrene-like intermediates for these reactions was *N*-acetoxyaminoquinazolone, [1.34]<sup>60,62,63</sup>. Such reagents when oxidised with lead tetraacetate in the presence of alkenes gives aziridines in good yield<sup>64</sup>. These yields are further improved by carrying out the oxidation in the presence of trifluoroacetic acid<sup>62,63</sup>. When trifluoroacetic acid was present, the stereoselectivity of the reaction is improved also. In addition, the reaction could be carried out at a lower temperature (causing a further improvement in asymmetric induction), and only equimolar quantities of the alkene were required to obtain good yields. This effect was explained in terms of a change in transition state geometry when the nitrene was protonated at the N-1 position of the quinazolone ring<sup>62</sup>.

Subsequent to this work the same author reported the use of an *N*-acetoxyaminoquinazolone reagent in the stereoselective synthesis of silylaziridines<sup>65,66</sup>. The *N*-acetoxyaminoquinazolone, [1.34] (Scheme 1.19) for the reaction is prepared *in situ* from the *N*-aminoquinazolone by oxidation with lead tetraacetate, in the absence of acid. Subsequent addition of the alkenylsilane leads to the formation of the aziridine, e.g., [1.35].



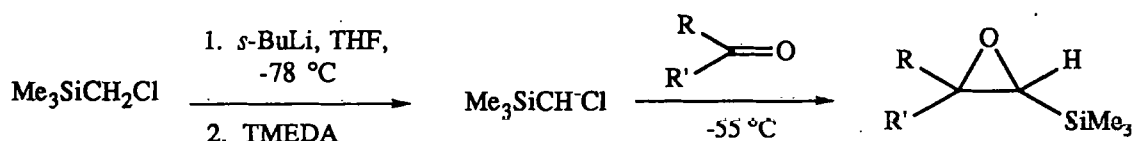
Scheme 1.19

Reactions were carried out using pure *trans*-trimethylsilylstyrene,  $\alpha$ -trimethylsilylstyrene and a *cis/trans* mixture of  $\alpha$ -trimethylsilyl- $\beta$ -methylstyrene. The relative yields obtained

are indicative that the reaction is sensitive to the degree of coplanarity which the phenyl group has with the double bond. This is explained in terms of a favourable interaction between the phenyl group and the quinazolone ring<sup>67</sup>. Such a conformation is readily attained in the case of *trans*- $\beta$ -trimethylsilylstyrene resulting in a high yielding (86%) reaction. Atkinson also reported the first successful silylaziridine fluorodesilylation with electrophilic capture<sup>68</sup>. This will be discussed in Chapter 4.

### 1.3.5 Syntheses of silylaziridines by the reaction of $\alpha$ -silyl carbanions with imines

Soobramanien<sup>29</sup> has prepared 2-trimethylsilylaziridines by the reaction of  $\alpha$ -silyl carbanions with imines. The precursor,  $\alpha$ -chloro- $\alpha$ -trimethylsilyl carbanion had previously been used by Magnus<sup>16</sup> as a precursor to silylepoxydes via its reaction with aldehydes and ketones as shown in Scheme 1.20.

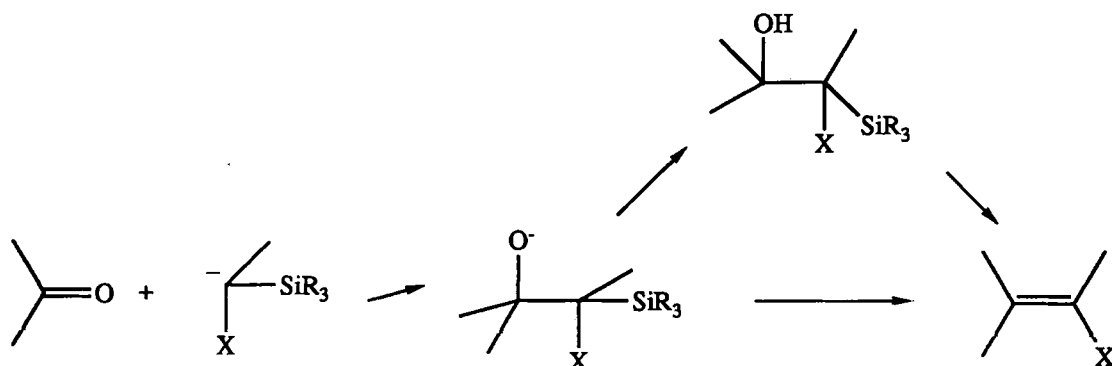


Scheme 1.20

Here the starting reagent,  $\alpha$ -chloromethyltrimethylsilane is deprotonated by treatment with *s*-butyllithium in THF containing one equivalent of tetramethylethylenediamine (TMEDA) at  $-78^\circ\text{C}$ . The so produced anion is then reacted with a suitable carbonyl compound generating the corresponding silylepoxyde.

This represents a very important synthesis since all previous methods used to produce silylepoxydes proceeded essentially via the epoxidation of vinylsilanes<sup>15</sup>. Although relatively facile and versatile, the method is not stereoselective, producing a mixture of *cis* and *trans* epoxides where R and R' differ.

$\alpha$ -Silyl carbanions are perhaps more commonly known as reagents in the Peterson Olefination<sup>69</sup> reaction where they are reacted with carbonyl compounds (Scheme 1.21). This method provides a route to a diverse range of substituted alkenes.

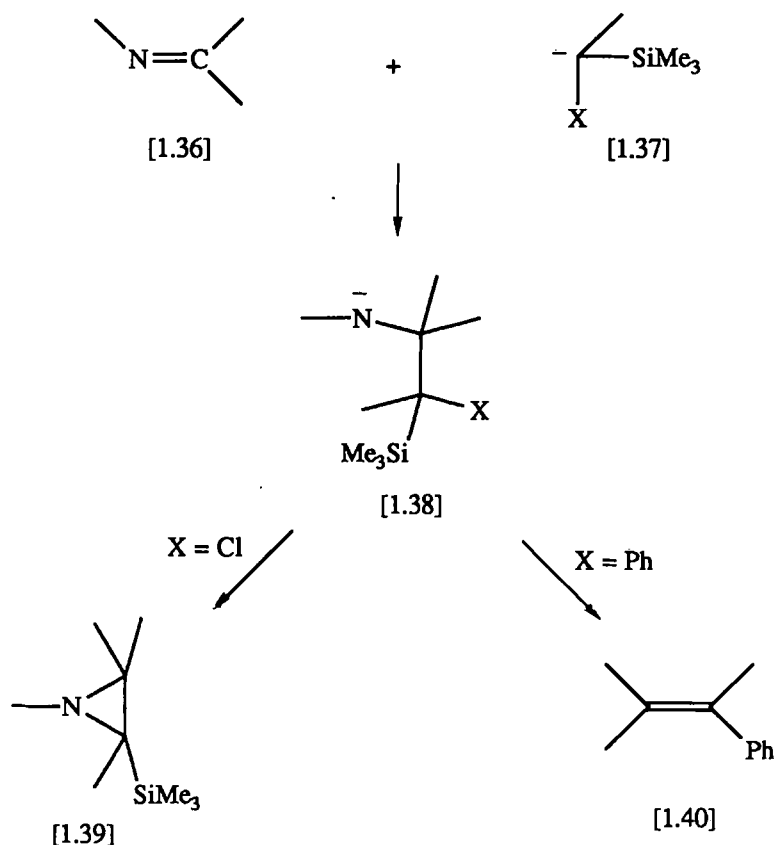


**Scheme 1.21** Peterson Olefination Reaction

When the substituent X does not have a stabilising effect on the anion, the  $\beta$ -hydroxysilane can often be isolated. It can then be converted to the alkene by treatment with acid or base.

A modified form of the Peterson reaction was applied in Soobramanien's synthesis of silylaziridines, [1.39] from imines, [1.36] as shown in Scheme 1.22. Here attack of the  $\alpha$ -chloromethyltrimethylsilyl carbanion, [1.37] at the carbon atom of the imine, [1.36] leads to an intermediate, [1.38] which readily cyclized to an aziridine, [1.39]. The chlorine atom on the  $\alpha$ -carbon in the transition state facilitates intramolecular cyclization rather than elimination of a  $\beta$ -aminosilane, (as is the case when the chlorine atom is replaced by a phenyl group) which would be analogous to the Peterson reaction leading to alkenes, [1.40].



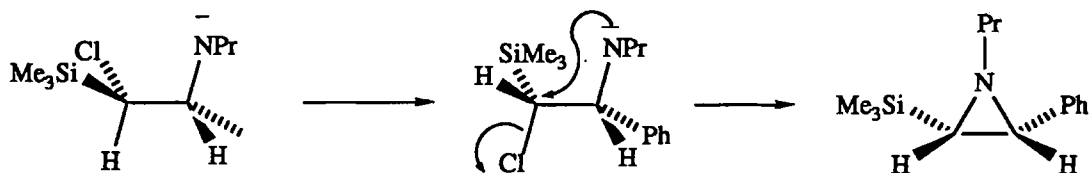


Scheme 1.22

The precursor  $\alpha$ -chloro- $\alpha$ -trimethylsilyl carbanion for the reaction is generated using a strong base, *s*-butyllithium in the presence of tetramethylethylenediamine (which acts as a chelating reagent towards the lithium ion). The anion, which is stable below  $-60\text{ }^{\circ}\text{C}$  condenses with imines to give an intermediate in which the nitrogen carries a negative charge. Cyclization occurs by intramolecular nucleophilic attack of the nitrogen anion with displacement of chloride ion and inversion of configuration to generate the 2-trimethylsilylaziridine.

With the aliphatic imine, *N*-benzylidenepropylamine the *cis* aziridine is formed stereospecifically, whereas the aromatic imine, *N*-benzylideneaniline led to a mixture (1:1) of *cis* and *trans* isomers. Stereocontrol in each case can be rationalised by examining the transition state leading to the intermediate. Using Bassindale and Taylor's approach control model<sup>70</sup> we can explain the formation of the intermediate which leads to the stereospecific formation of the *cis* aziridine via an elimination in which the C-N and C-Cl

bonds are *trans* coplanar and the phenyl and trimethylsilyl groups are *syn* related (Scheme 1.23).



Scheme 1.23

## 1.4 References

1. C. Friedel and J.M. Crafts, *Ann.*, **136**, 203, (1865).
2. L. Pauling, "The Nature of the Chemical Bond and the Structure of Molecules and Crystals", 3rd edn., Cornell Univ. Press, Ithaca, New York, 1960 p. 88-99.
3. E.A.V. Ebsworth, "Organometallic Compounds of the Group IV Elements", Vol. 1, Ed., A.G. MacDiarmid, Dekker, New York, 1968, p. 1-104.
4. C. Eaborn, "Organosilicon Compounds", Butterworths, London, 1960, Chapter 3.
5. I. Fleming A. Pearce and R.L. Snowden, *J. Chem. Soc., Chem. Commun.*, **182**, (1976).
6. J.J. Eisch and J.E. Galle, *J. Am. Chem. Soc.*, **98**, 4646, (1976).
7. E. Colvin, "Silicon in Organic Synthesis", Butterworths, 1981, Chapter 3.
8. A.W.P. Jarvie, A. Holt and J. Thomson, *J. Chem. Soc. B*, **852**, (1969).
9. M.A. Cook, C. Eaborn and D.R.M. Walton, *J. Organomet. Chem.*, **24**, 293, (1970).
10. R.W. Bott. C. Eaborn and P.M. Greasley, *J. Chem. Soc.*, **4804**, (1964).
11. T.G. Traylor, W. Hanstein, H.J. Berwin, N.A. Clinton and R.S. Brown, *J. Am. Chem. Soc.*, **93**, 5715, (1971).
12. R.E. Parker and N.S. Isaacs, *Chem. Rev.*, **59**, 737, (1959).
13. G. Stork and E. Colvin, *J. Am. Chem. Soc.*, **93**, 2080, (1971).
14. P.F. Hudrlik, A.M. Hudrlik, R.J. Rona, R.N. Misra and G.P. Withers, *J. Am. Chem. Soc.*, **99**, 1993, (1977).
15. J.J. Eisch and J.T. Trainor, *J. Org. Chem.*, **28**, 487, (1963).
16. C. Burford, F. Cook, E. Ehlinger and P. Magnus, *J. Am. Chem. Soc.*, **99**, 4536, (1977).
17. Plesnicar, "Oxidation in Organic Chemistry", Ed. Trahanovski, Academic Press, New York, 1978, p. 211.
18. T. Katsuki, and K.B. Sharpless, *J. Am. Chem. Soc.*, **102**, 5974, (1980).
19. T.B.E. Rossiter, T. Katsuki, and K.B. Sharpless, *J. Am. Chem. Soc.*, **103**, 464,

- (1981).
20. V.S. Martin, S.S. Woodward, T. Katsuki, Y. Yamada, M. Ikada and K.B. Sharpless, *J. Am. Chem. Soc.*, **103**, 6237, (1981).
  21. H. Tomioka, T. Suzuki, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, 3387, (1982).
  22. J.J. Eisch and J.T. Trainor, *J. Org. Chem.*, **28**, 2870, (1963).
  23. J.J. Eisch and J.E. Galle, *J. Org. Chem.*, **41**, 2615, (1976)
  24. P.F. Hudrlik, R.N. Misra, G.P. Withers A.M. Hudrlik, R.J. Rona, and J.P. Arcoleo, *Tetrahedron Lett.*, 1453, (1976).
  25. P.F. Hudrlik, J.P. Arcoleo, R.H. Schwartz, R.N. Misra, and R.J. Rona, *Tetrahedron Lett.*, 591, (1977).
  26. P.F. Hudrlik, A.M. Hudrlik, R.N. Misra, D. Peterson, G.P. Withers and A.K. Kulkarni, *J. Org. Chem.*, **45**, 4444, (1980).
  27. G.Berti, S. Canedoli, P. Crotti, F. Macchia, *J. Chem. Soc. Perkin. Trans. I*, 1183, (1984).
  28. S.G. Wierschke, J. Chandrasekhar and W.L. Jorgensen, *J. Am. Chem. Soc.*, **107**, 1496, (1985).
  29. M.C.C. Soobramanien, Ph.D. Thesis, The Open University, Milton Keynes, (1988).
  30. J.J. Eisch and J.E. Galle, *J. Organomet. Chem.*, **121**, C10-C14, (1976).
  31. J.J. Eisch and J.E. Galle, *J. Organomet. Chem.*, **341**, 293, (1988).
  32. G.A. Molander and K. Mautner, *J. Org. Chem.*, **54**, 4042, (1989).
  33. K.A. Adrianov, V.I. Sidorov and L.M. Khananashvili, *Dolk. Akad. Nauk. SSSR*, **158**, 868, (1964).
  34. K.A. Adrianov, V.I. Sidorov and L.M. Khananashvili, *J. Gen. Chem. USSR*, **36**, 178, (1966).
  35. T. Sheradsky "The Chemistry of the Azido Group", Ed. S. Patai, Wiley (Interscience) New York, 1971, p. 331.
  36. R. Huisgen, L. Mobius, G. Mueller, H. Stangl, G. Szeimies and J.M. Vernon,

- Chem. Ber.*, **98**, 3392 (1965).
37. P. Scheiner, J.H. Schomaker, S. Deming, W.J. Libbey and G.P. Nowak, *J. Am. Chem. Soc.*, **87**, 306, (1965).
  38. R. Huisgen and G. Szeimies, *Chem. Ber.*, **98**, 1153, (1965).
  39. R. Huisgen, G. Szeimies and L. Mobius, *Chem. Ber.*, **100**, 2494 (1967).
  40. G.D. Buckley, *J. Chem. Soc.*, 1850, (1954).
  41. R. Huisgen, R. Grashey and J. Sauer in "The Chemistry of Alkenes", Ed. S. Patai, Wiley (Interscience), New York, 1964, p. 835.
  42. P. Scheiner in "Selective Organic Transformations", Ed. B.S. Thyagarajan, Wiley (Interscience), New York, 1970, p. 327.
  43. F. Texier and R. Carrie, *Bull. Soc. Chim. Fr.*, 3642, (1971).
  44. E. Ettenhuber and K. Ruhlmann, *Chem Ber.*, **101**, 743, (1968).
  45. A.R. Bassindale, A.G. Brook, P.F. Jones and J.A.G. Stewart, *J. Organomet. Chem.*, **152**, C 25-28, (1978).
  46. P. Zanirato, *J. Chem. Soc., Perkin Trans 1*, 2789, (1991).
  47. F. Duboudin, *J. Organomet. Chem.*, **174**, C 18-20, (1979).
  48. F. Duboudin, *J. Organomet. Chem.*, **156**, C 25-28, (1978).
  49. E.J. Thomas and G.H. Whitham, *J. Chem. Soc., Chem. Commun.*, 212, (1979).
  50. E.J. Grayson and G.H. Whitham, *Tetrahedron*, **44**, 4087, (1988).
  51. E. Lukevics, V.V. Dirnens, Y.S. Goldberg, E.E. Liepinsh, I.Y. Kalvinsh, and M.V. Shymanska, *J. Organomet. Chem.*, C 29-32, 268, (1984).
  52. R.S. Neale, *Synthesis*, 1, (1971).
  53. T.P. Sneden, and R.W. Turner, *J. Chem. Soc.*, 876 (1968).
  54. N.A. Rybakova, P.V. Petrovsky, P.O. Okulevich and R. Freidlinda, *Kh. Izv. Akad. Nauk SSSR Ser. Khim.*, 1574, (1970).
  55. E. Lukevics, V.V. Dirnens, Y.S. Goldberg and E.E. Liepinsh, *J. Organomet. Chem.*, **316**, 249, (1986).
  56. W. Lwowski and T.W. Mattingly, *J. Am. Chem. Soc.*, **87**, 1947, (1965).
  57. W. Lwowski and T.J. Maricich, *J. Am. Chem. Soc.*, **87**, 3630, (1965).

58. J.S. McConaghy and W. Lwowski, *J. Am. Chem. Soc.*, **89**, 4450, (1967).
59. W. Lwowski, F.P. Woerner, *J. Am. Chem. Soc.*, **87**, 5491, (1965).
60. R.S. Atkinson, J. Fawcett, D.R. Russell, and G. Tughan, *J. Chem. Soc., Chem. Commun.*, 832, (1986).
61. R.S. Atkinson, and G. Tughan, *J. Chem. Soc., Chem. Commun.*, 834, (1986).
62. R.S. Atkinson, and G. Tughan, *J. Chem., Soc., Chem. Commun.*, 456, (1987)
63. R.S. Atkinson, C.M. Darrah, and B.J. Kelly, *Tetrahedron Lett.*, 1711, (1987).
64. R.S. Atkinson, "Azides and Nitrenes", Ed. E.F.V. Scriven, Academic Press, Orlando, Florida, 1984.
65. R.S. Atkinson, and B.J. Kelly, *J. Chem., Soc., Chem. Commun.*, 836, (1989).
66. R.S. Atkinson, and B.J. Kelly, *J. Chem., Soc., Perkin Trans. 1*, 1657, (1986).
67. R.S. Atkinson, and J.R. Malpass, *J. Chem. Soc.*, 2242, (1977).
68. R.S. Atkinson and B.J. Kelly, *Tetrahedron Lett.*, 2703, (1989).
69. D.J. Peterson, *J. Org. Chem.*, **33**, 780, (1967).
70. A.R. Bassindale, R.J. Ellis, J.C.Y. Lau and P.G. Taylor, *J. Chem. Soc., Chem. Commun.*, 98, (1986).

## CHAPTER 2

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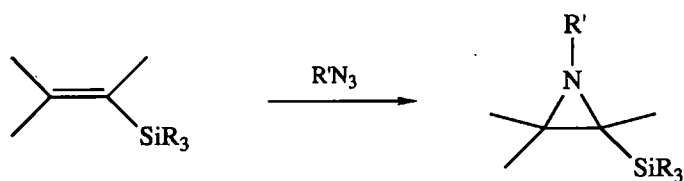
### SILYLAZIRIDINES : NEW SYNTHETIC METHODS

#### 2.1 Introduction

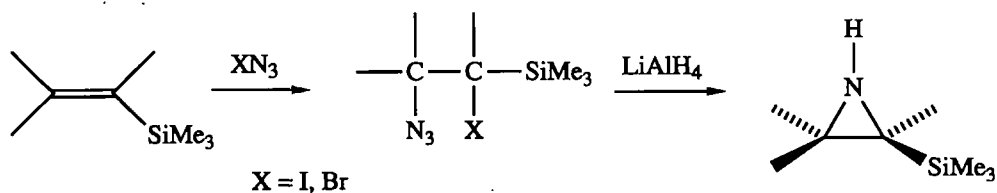
##### 2.1.1 Previous syntheses of silylaziridines

Aziridines containing a carbon-silicon bond, although potentially very useful intermediates, have enjoyed conspicuously little coverage in the literature. Whereas the epoxy analogues are relatively easily prepared, predominantly by oxidation of vinylsilanes, there are very few generally applicable syntheses of silylaziridines. These have been described in some detail in the previous Chapter and are summarized below.

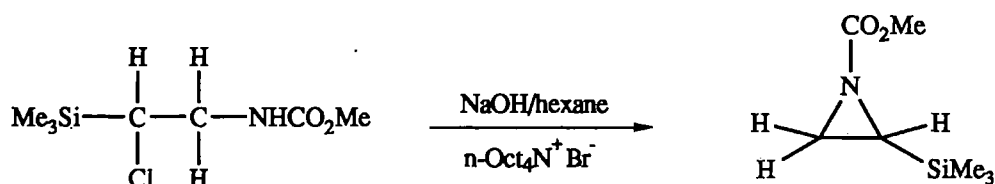
1. Thermal/photochemical decomposition of arylazides in the presence of vinylsilanes<sup>1,2</sup>.



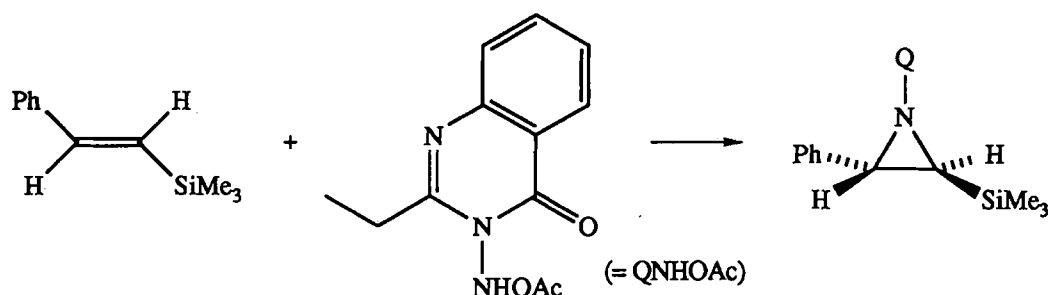
2. Reduction of haloazides derived from vinylsilanes<sup>3-6</sup>.



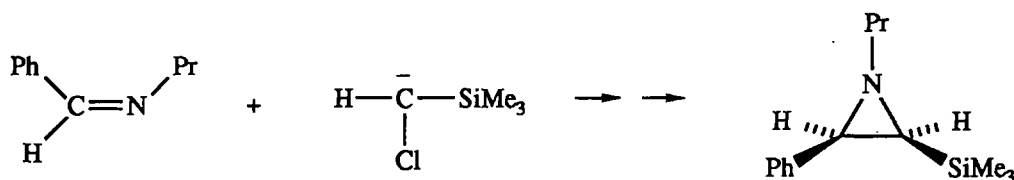
3. Intramolecular alkylation of alkyl *N*-[2-chloro-2-(trialkylsilyl)ethyl]carbamates under solid-liquid phase transfer conditions<sup>7</sup>.



4. Reaction of vinylsilanes with *N*-acetoxyaminoquinazalone<sup>8</sup>.



5. Condensation of  $\alpha$ -chloromethylenetriethylsilyl anions with imines<sup>9</sup>.



### 2.1.2 New routes to silylaziridines

Three routes to silylaziridines have been developed during the course of the current study, all of which are generally applicable, and have been used to prepare a series of previously unknown silylaziridines. In summary, these are: the thermal reaction between phenyl azide and functionalized vinylsilanes (section 2.2.1); reduction of bromoazides derived from vinylsilanes (section 2.2.2) and photolysis of ethyl or methyl azidoformate in the presence



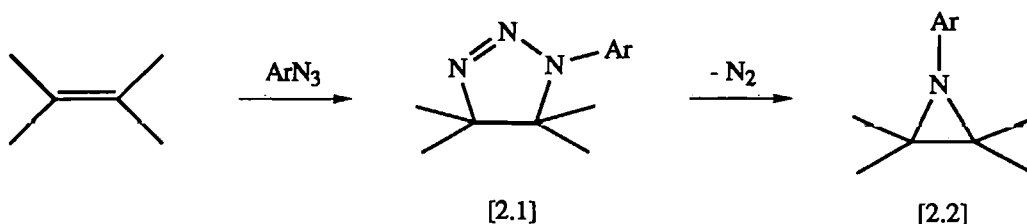
of vinylsilanes (section 2.2.3). Silylaziridines were also synthesized by ring preserving reactions of parent silylaziridines. Some details of this method are given in section 2.2.4, however, these reactions are discussed at greater length in Chapter 3.

In the current work we have synthesized a series of functionalized silylaziridines by the thermal reaction of phenyl azide with functionalized vinylsilanes. Also, we have extended the work of Duboudin on the reduction of haloazides, and shown that it constitutes a generally applicable synthesis of silylaziridines. Furthermore, contrary to the findings of Duboudin, it has been shown that by changing the conditions, the course of the reaction with *trans*-trimethylsilylstyrene may be altered in favour of producing either the RS/SR or SS/RR bromoazide leading on reduction to the *cis* or *trans* aziridines respectively. This reaction constitutes a good illustration of the directive power of silicon. Finally, a series of silylaziridines has been synthesized by the addition of photochemically generated carboethoxy (and carbomethoxy) nitrenes to vinylsilanes. Although Lukevics has described alternative routes to similar silylaziridines, this method is much more convenient in that it is a one step reaction and gives much cleaner products and higher yields. Also this method is more versatile in that a variety of vinylsilanes will form adducts with the nitrene.

## 2.2 Preparative and mechanistic aspects of silylaziridine synthesis

### 2.2.1 The thermal reaction of phenyl azide in the presence of vinylsilanes

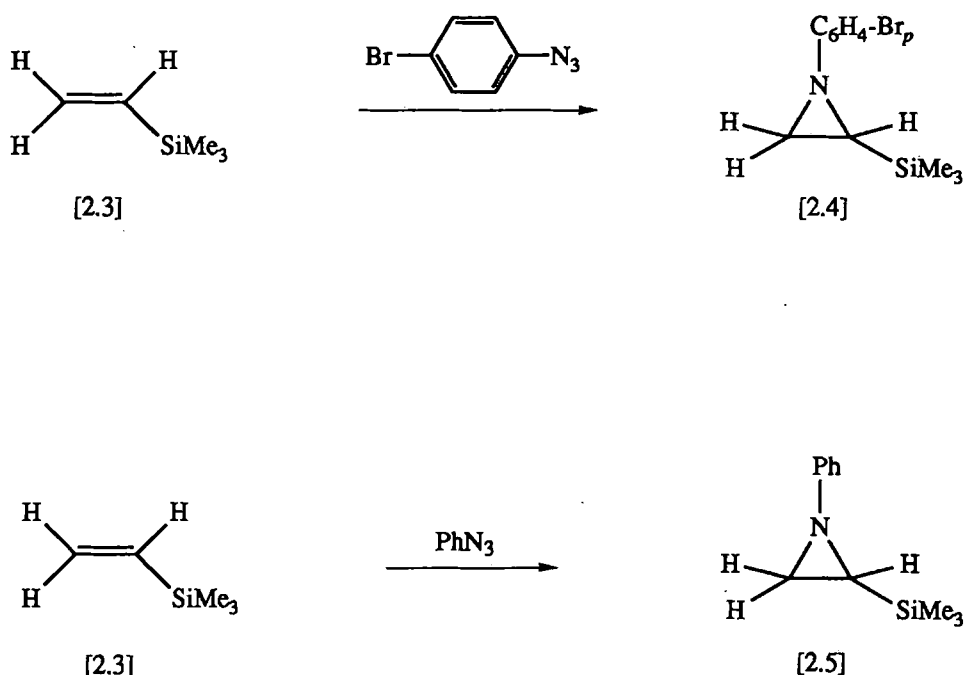
A commonly used general method of synthesizing aziridines is the reaction of arylazides with alkenes.



Scheme 2.1

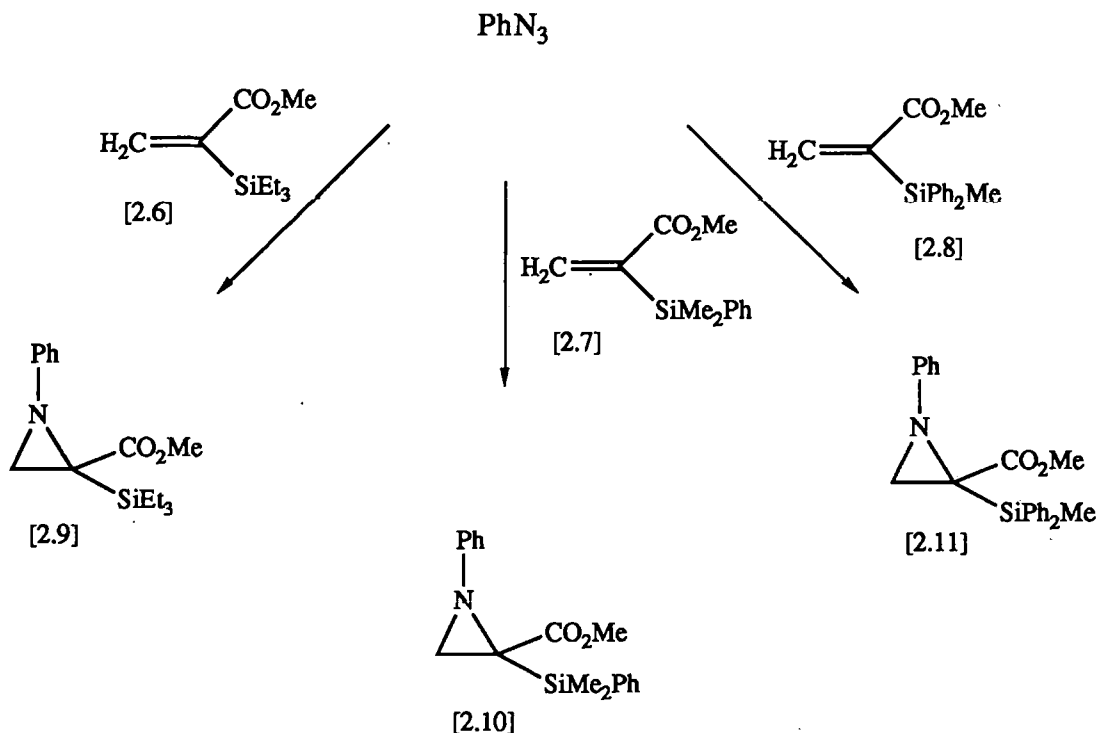
This leads initially to the formation of the corresponding triazoline, [2.1] which may be decomposed subsequently to yield the aziridine, [2.2] by either photochemical or thermal means (Scheme 2.1). This method of aziridine synthesis has been discussed in more detail in Chapter 1.

Bassindale<sup>1</sup> and co-workers have applied this method in the synthesis of silyl substituted aziridines. They report that phenyl azide and *para* substituted phenyl azides react thermally with vinylsilanes, e.g. [2.3], to produce *N*-arylsilylaziridines, in this case, [2.4] and [2.5], (Scheme 2.2).



Scheme 2.2

In the current work, several new silylaziridines [2.9], [2.10] and [2.11] have been synthesized by the thermal reaction of phenyl azide in the presence of functionalized vinylsilanes [2.6], [2.7] and [2.8] (Scheme 2.3). The chemistry of these aziridines has been explored in some detail, in particular, their reactivity towards fluoride ion, as will be discussed in Chapter 4.

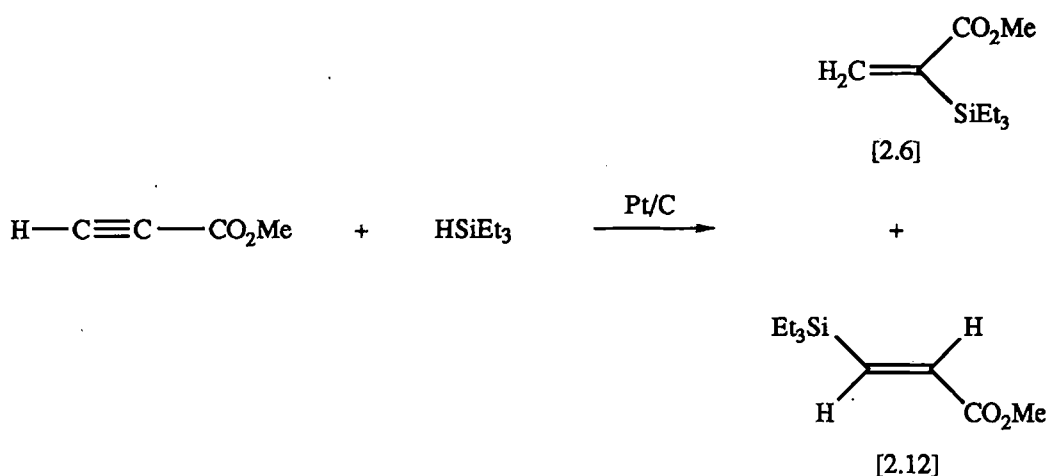


Scheme 2.3

Aziridines can be classed into two groups, basic aziridines and those which possess an activating substituent on nitrogen - activated aziridines<sup>10</sup>. Aziridines bearing a phenyl group on nitrogen are activated towards nucleophilic ring opening, owing to the ability of the phenyl group to delocalize the charge which builds up on the aziridine nitrogen in the transition state when the compound reacts with a nucleophile. Indeed *N*-aryl aziridines undergo nucleophilic ring opening with relative ease. Similarly, silylaziridines bearing an *N*-carboethoxy substituent might be expected to undergo facile fluorodesilylation. However, repeated attempts to desilylate such an aziridine have failed. It was this finding, that prompted the search for a silylaziridine which was more activated and might undergo desilylation more readily. It was postulated that an aziridine bearing an ester substituent on the same carbon as the silicon moiety would be especially susceptible to desilylation, since negative charge build up on the  $\alpha$  carbon in the transition state might be stabilized by conjugation with the carbonyl group<sup>§</sup>. A method was therefore developed for the

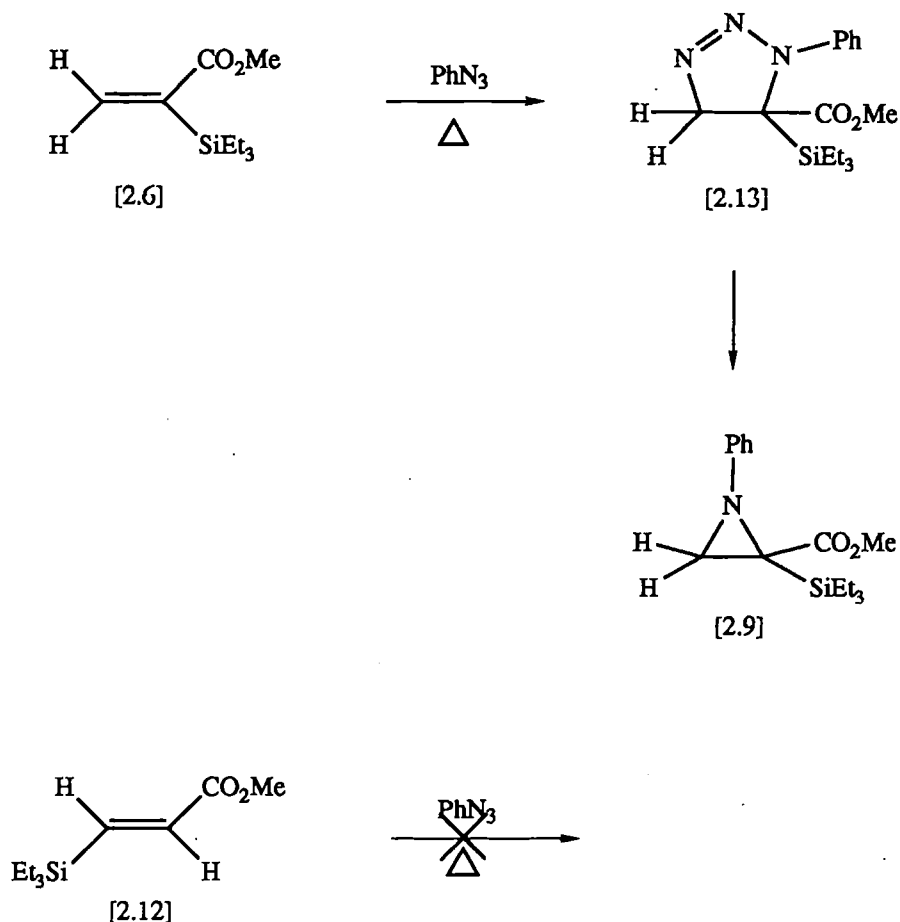
<sup>§</sup> Subsequent studies revealed that this rationale for fluorodesilylation may be invalid.

synthesis of such an aziridine. The route which had been considered first was the thermal reaction of phenyl azide and vinylsilanes. Methyl 2-(triethylsilyl)propenoate, [2.6] was chosen since a convenient preparation, by hydrosilylation of methyl propynoate, is reported in the literature<sup>11</sup>. The desired vinylsilane was formed in 30% yield (70% is the *vicinal* regioisomer, [2.12]) using the method of Lukevics who actually reports that the *geminal* isomer [2.6], is the major (70%) product. It was found however, that the yield could be increased to 70% in favour of the *geminal* isomer when 10% platinum on carbon was used as the catalyst (Scheme 2.4). The two regioisomers can be separated by column chromatography on silica. However, in most cases a partially purified mixture of [2.6] and [2.12] was used to prepare the aziridine.



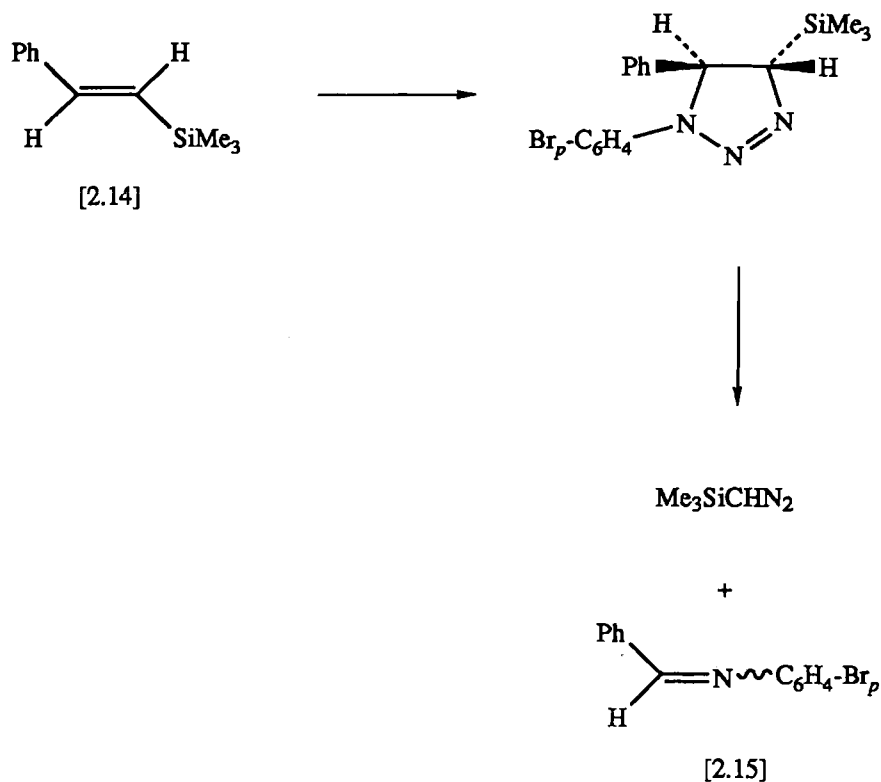
Scheme 2.4

The aziridine was made by heating a mixture of phenyl azide and [2.6] at 120 °C in the absence of solvent and the reaction was generally complete within 2 hours. When a mixture of the two regioisomeric vinylsilanes was used, addition to the *geminal* isomer [2.6] only is observed, the *vicinal* isomer, [2.12] failing to produce an aziridine (Scheme 2.5). Consequently the required product, [2.9] could be obtained easily in pure form by column chromatography of the product mixture.



**Scheme 2.5**

There is no clear explanation for the observed selectivity although it may be due to electronic factors in the formation of an intermediate triazoline. There was no evidence from NMR spectra for the intermediacy of a triazoline (possibly due to very rapid decomposition to the aziridine). After partial reaction, the product mixture consisted of aziridine and the starting alkene only. Also, no retro-addition product was formed during the reaction as has been reported<sup>1</sup> previously for the reaction of *trans*-trimethylsilylstyrene, [2.14] with *para*-bromophenyl azide which gives the enamine [2.15], Scheme 2.6.

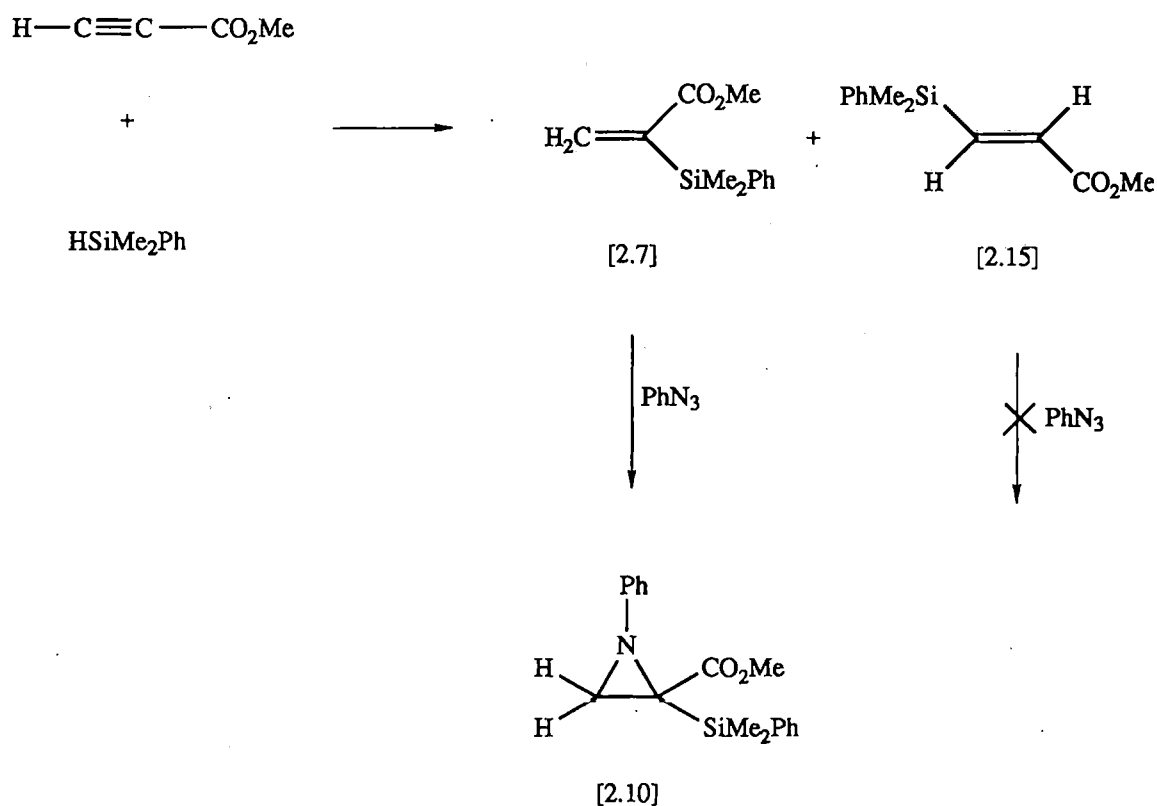


Scheme 2.6

The reactivity of this aziridine, [2.9] was explored. The reaction with fluoride ion was of particular interest and also nucleophilic ring opening. It was found that the aziridine could be fluorodesilylated readily as predicted, but all attempts to trap the so formed anion with electrophiles were unsuccessful. Possible reasons for the observed behaviour are discussed in Chapter 4.

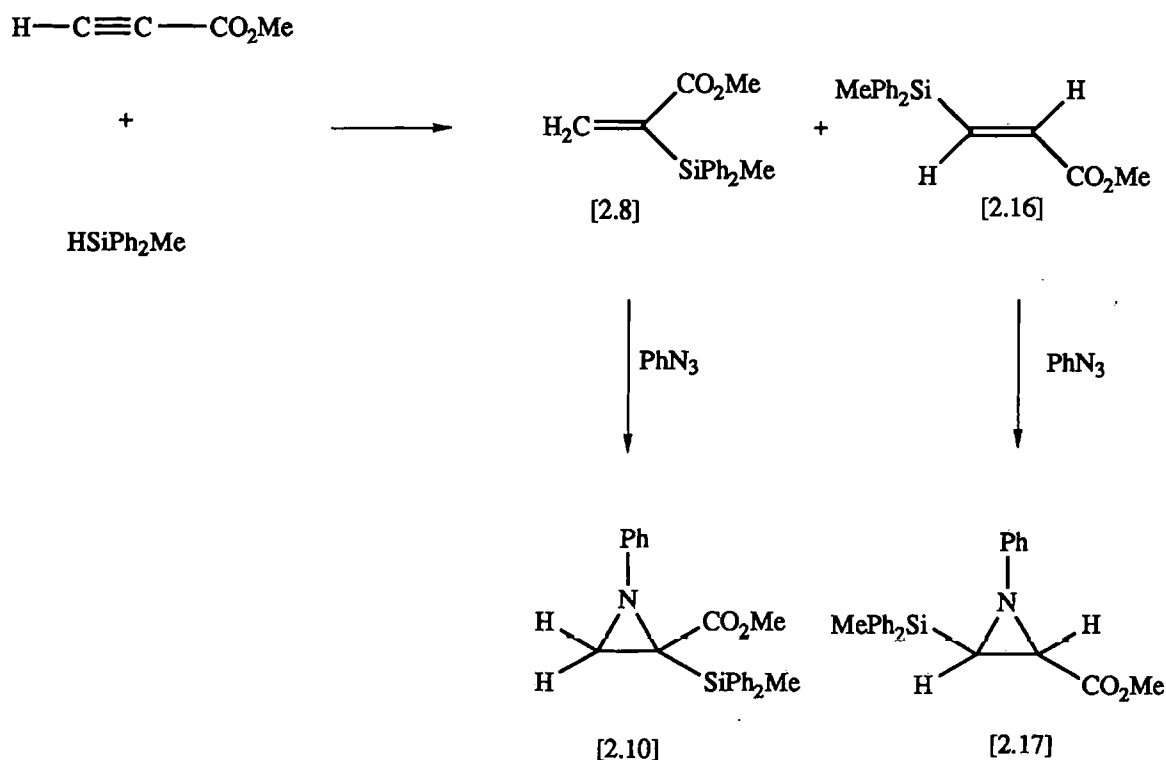
It was thought at this stage that the aziridine could be further activated, such that the anion might be trapped, by replacing the triethylsilyl group by a dimethylphenylsilyl or diphenylmethylsilyl group. These aziridines were correspondingly synthesized by thermolysis of phenyl azide in the presence of the appropriate vinylsilane (Schemes 2.7 and 2.8). The vinylsilanes were synthesized by hydrosilylation of methyl propynoate again in the presence of a platinum on carbon catalyst. In each case a mixture of regioisomers was generated, 70% in favour of the *geminal* isomer with dimethylphenylsilane and 60% with diphenylmethylsilane.

Phenyl azide was found to react selectively with the *geminal* isomer methyl 2-(dimethyl-phenylsilyl)propenoate, [2.7], when a mixture of regioisomers [2.7] and [2.15] was used, to form the corresponding aziridine [2.10], Scheme 2.7.



Scheme 2.7

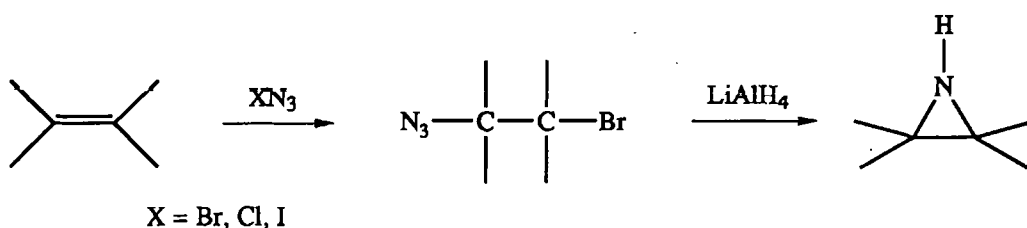
However, the reaction was non-selective with the diphenylmethylsilylalkenes, [2.8] and [2.16]. In this case, both alkenes reacted with the phenyl azide to produce the corresponding aziridines (Scheme 2.8). These could not be separated by chromatography. Since it was also almost impossible to separate the regioisomeric vinylsilanes, this aziridination was not studied further.



Scheme 2.8

### 2.2.2 The preparation of silylaziridines by reduction of silyl substituted bromoazides

The reaction of alkenes with bromine, iodine and chlorine azides has been known for some time<sup>12</sup>. The resultant  $\beta$ -haloazides can be reduced stereospecifically to aziridines with lithium aluminium hydride<sup>13</sup>, (Scheme 2.9).



Scheme 2.9

To provide a route to *N*-unsubstituted silylaziridines, we examined the reaction between bromine azide and vinylsilanes. Duboudin<sup>3,4</sup> first used this route and we have been able to

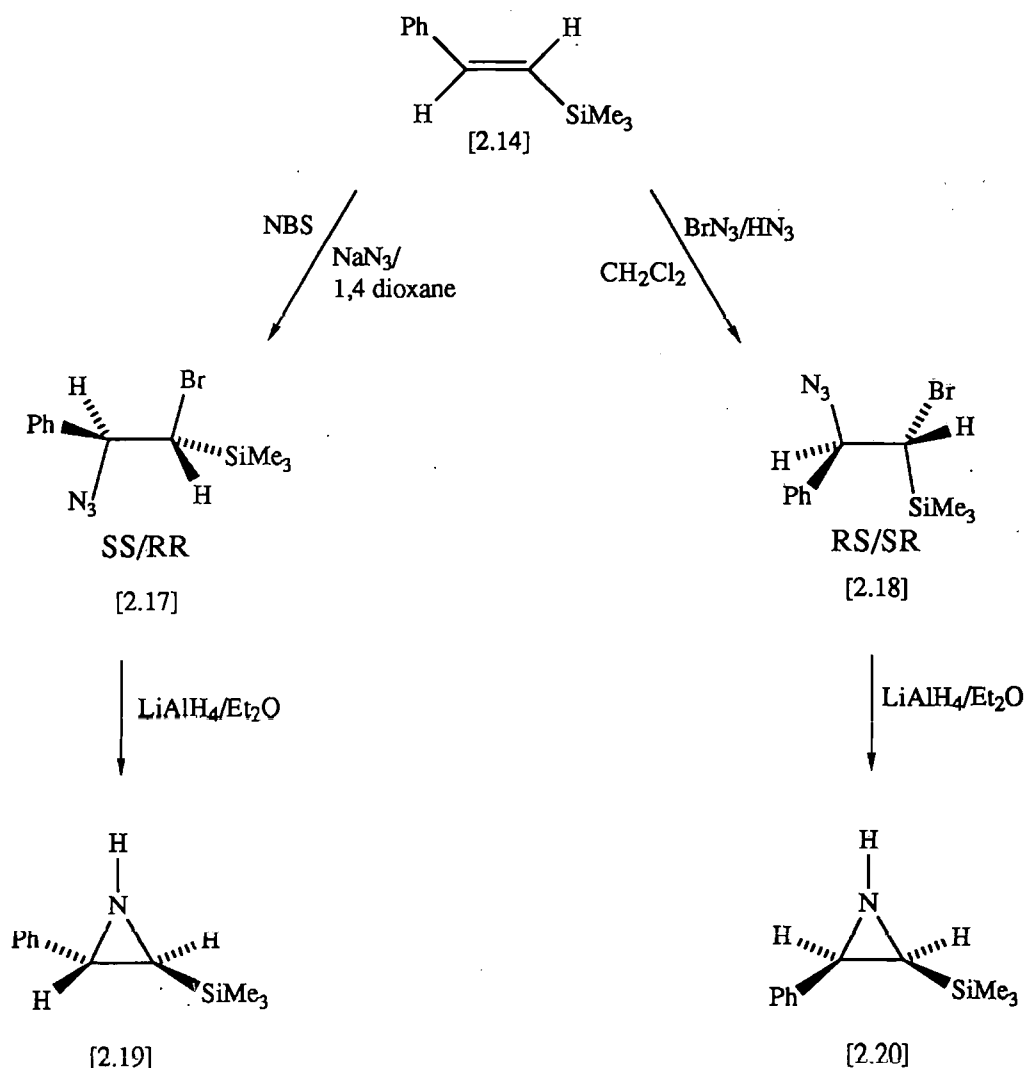


extend it leading to a range of silylaziridines. In particular we found that by altering the conditions it was possible to make either the *cis* or *trans* aziridine from the same starting alkene.

#### 2.2.2.1 Stereocontrol in the synthesis of bromoazides from *trans*-trimethylsilylstyrene

Addition of bromine azide to *trans*-trimethylsilylstyrene, [2.14] can lead to four stereoisomeric adducts, as RS/SR, [2.18], and SS/RR, [2.17], enantiomeric pairs.

Depending on the method chosen, it was possible to synthesize in good yield either the RS/SR or the SS/RR adducts selectively. These on reduction gave the corresponding *cis*, [2.20] and *trans* aziridines, [2.19] respectively (Scheme 2.10).



Scheme 2.10

The mechanism for bromine azide addition is dependent on the reaction conditions and dictates stereochemical outcome. The regiochemistry of bromine azide addition can be predicted from consideration of the mechanism, the aspects of which are already well established in the literature. We would predict that the preferred regiochemistry for addition of bromine azide would be such that the azide function becomes attached to the carbon  $\beta$  to silicon. Indeed Witham<sup>6</sup> has shown that the addition of iodine azide to cyclic vinylsilanes occurs with high regio and stereoselectivity. The details of this reaction were discussed in Chapter 1. Similarly, reactions with other iodine based electrophilic reagents also gave rise to the same regiochemistry.

Further evidence for the proposed regiochemistry in this system, and some other bromoazide systems can be drawn from a comparison of the carbon NMR shifts of the bromoazides with those of azido alcohols which have the opposite regiochemistry. The data is given in Table 2.1 below.

**Table 2.1**  $^{13}\text{C}$  NMR data of silylated azido compounds

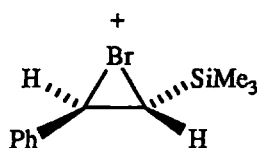
Azido compound	Chemical shift	
	C-Si	C-CSi
1-trimethylsilyl-1-azido-2-hydroxy hexane	61.1	73.4
1-trimethylsilyl-1-azido-2-hydroxy-2-phenyl ethane	60.3	75.2
2-azido-1-bromo-1-trimethylsilyl pentane	45.7	65.3
2-azido-1-bromo-1-trimethylsilyl hexane	47.8	67.7
2-azido-1-bromo-2-phenyl-1-trimethylsilyl ethane	47.4	69.9

The disparity in chemical shifts suggests that the azido alcohols and the bromoazides have opposite regiochemistry. The azido alcohols were obtained by electrophilic ring opening of the corresponding silylepoxides using hydrazoic acid. In this case ring opening occurs by a different mechanism (as described in Chapter 1, section 1.2.3) leading to  $\alpha$  ring cleavage. The mechanism for the formation of silyl bromoazides will be discussed later in this section.

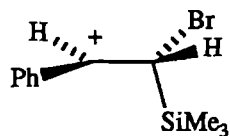
Two methods were used to generate the bromine azide for the reaction. One method involved the preparation of bromine azide *in situ* with the vinylsilane in a highly polar medium, a method similar to that of Van Ende<sup>14</sup>. This leads to an SS/RR bromoazide adduct, [2.17]. The other method<sup>15</sup> involved the addition of a preformed bromine azide/hydrazoic acid solution to a dichloromethane solution of the alkene leading to the RS/SR compound, [2.18].

Previous reports suggest that the synthesis of iodo or bromoazides from alkenes proceeds via an intermediate cyclic iodonium or bromonium ion<sup>16,17</sup>. The intermediacy of such a structure was first proposed<sup>17</sup> in order to rationalise the stereochemical outcome of alkene formation by elimination of HX. Fowler<sup>12</sup> has proposed that the halonium ion must have substantial carbocationic character. Except where steric hindrance forbids, ring opening by addition of nucleophiles always follows the Markownikov rule. Indeed, when *trans*-1-trimethylsilylhexene is treated with iodine azide, an adduct is obtained in which the iodo function is bonded to the carbon  $\alpha$  to silicon<sup>4</sup>. This is contrary to the observed regioselectivity of ring opening of epoxides. In this latter case the dominant effect is believed to be the stabilization of an incipient negative charge on a five-coordinate transition state. However with the halonium ion complex, carbon-halogen bond cleavage occurs ahead of nucleophile-carbon bond formation and the transition state enjoys stabilization from the silicon by the so called  $\beta$ -effect.

In the current work either the RS/SR or the SS/RR adduct is formed with at least 95% diastereoselectivity. In each case it is believed that an intermediate bromonium ion is formed and the stereochemical outcome depends on whether attack by azide ion precedes, or follows ring opening of the bromonium ion complex, that is, whether the nucleophile attacks the substrate in the form of a cyclic bromonium ion, or an open chain carbocation.



bromonium ion  
complex



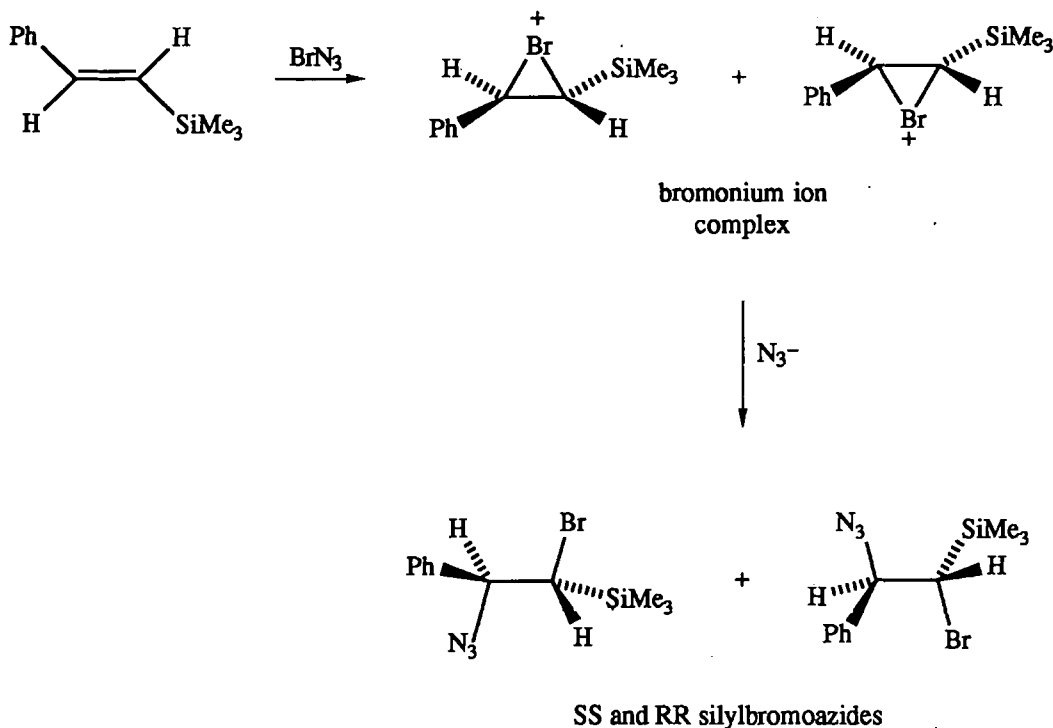
open chain  
carbocation

In the route to the SS/RR azide, [2.17], the bromonium ion donor, *N*-bromosuccinimide, is added in portions to an aqueous dioxane solution containing the alkene and a large excess of sodium azide. At any one time therefore, the concentration of azide ion vastly exceeds that of bromine azide. Also in such a medium the bromine azide molecule will be ionized.



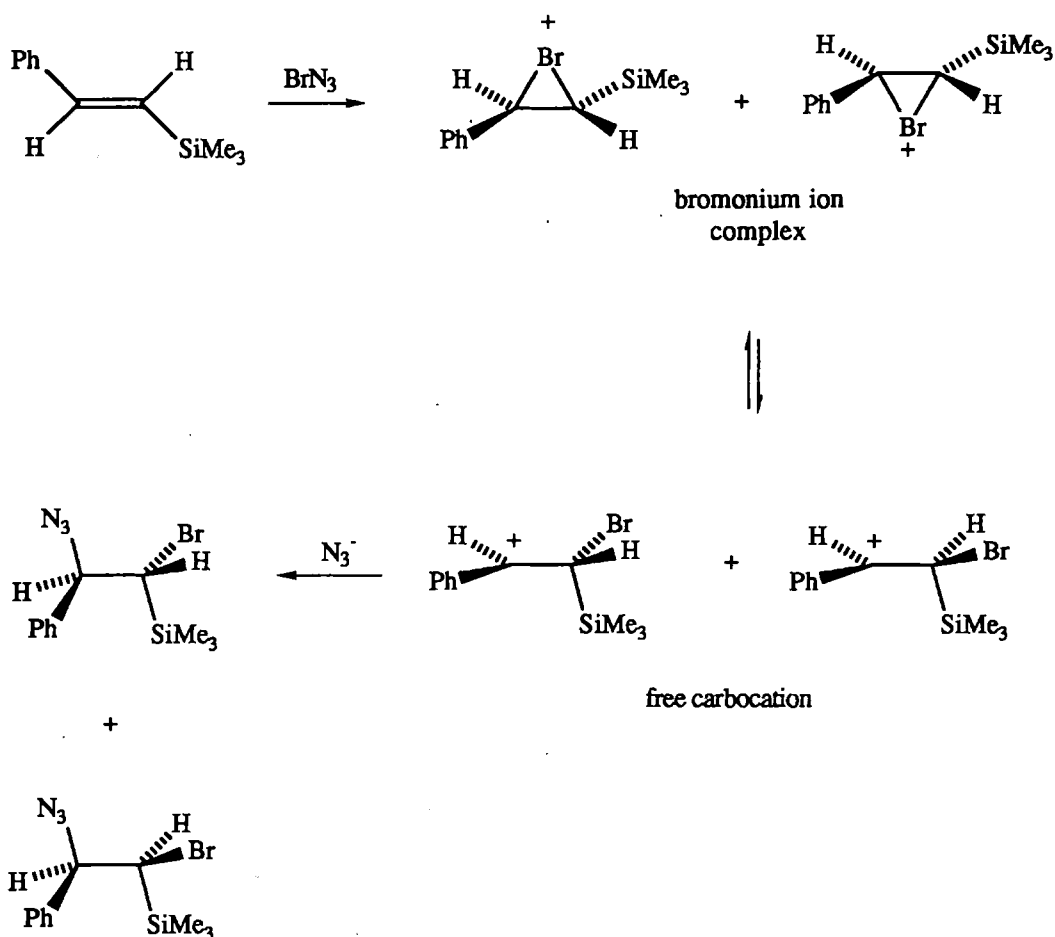
The lifetime of the bromonium ion before attack of azide is correspondingly short.

Nucleophilic ring opening occurs in a Markownikov fashion, that is,  $\beta$  to silicon and  $\alpha$  to the phenyl group. Two bromonium ions are possible leading to the SS and RR isomers (Scheme 2.11).



Scheme 2.11

The other route, which leads to the RS/SR diastereoisomers, involves the addition of a preformed dichloromethane solution of bromine azide and hydrazoic acid to the alkene at 0 °C, Scheme 2.12.



RS and SR silylbromoazides

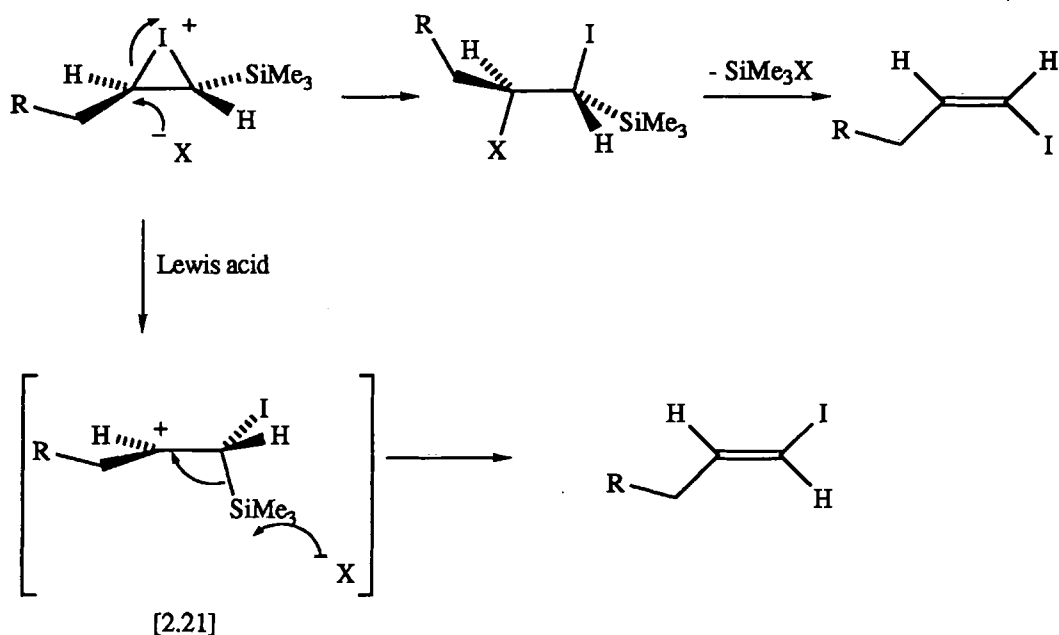
Scheme 2.12

Although the azide is in excess (in the form of hydrazoic acid), this is largely covalently bonded in dichloromethane, so the equilibrium concentration of azide ion will be relatively low (some dielectric constants are given in Table 2.2 below). Unless an excess of hydrazoic acid is used in the reaction, the dibromo adduct is formed. This can only be due to the presence of unreacted bromine in the dichloromethane layer.

**Table 2.2 Dielectric Constants of solvents**

solvent	$\epsilon_0$
H <sub>2</sub> O	78.54
1,4-dioxane	2.209
CH <sub>2</sub> Cl <sub>2</sub>	9.08

The silylbromoazide formed by this route does not result from attack on the cyclic bromonium ion, but on the free carbocation. Ring opening of the bromonium ion followed by least motion rotation so that the carbon-silicon bond is in line with the empty p orbital gives the carbocation. This is then attacked by azide ion from the least hindered side, that opposite the bulky trimethylsilyl group to give the RS/SR bromoazide (Scheme 2.12). Such a rationalisation is similar to that given by Chan<sup>18</sup> in his 'tuneable' stereoselective alkene synthesis using iododesilylation of vinylsilanes (Scheme 2.13).



**Scheme 2.13**

The presence of a Lewis acid diminishes the reactivity of X<sup>-</sup> resulting in the production of a transient carbonium ion species, [2.21].

This type of rationale is frequently used to explain why both retention and inversion is observed with addition/elimination reactions of vinylsilanes<sup>19</sup>. If such a rationale applies to the change in stereochemistry observed in our system, it implies that the reaction proceeds by a bromonium ion in 1,4-dioxane and via an open chain carbocation species in dichloromethane. Why a particular intermediate predominates in one solvent is difficult to predict. This will depend upon the relative stability of the carbocation versus the bromonium ion and the relative nucleophilicity of the azide ion in the two media. The results suggest that the carbocation is less stable in 1,4-dioxane and/or that the azide ion is less nucleophilic in dichloromethane. This balance between bromonium ion and open chain carbocation is clearly very delicate and also depends upon the substrate structure.

Our findings are contrary to those of Duboudin et al who report that the same azide (RS/SR) is produced when either of the two routes are employed. Also, she has been unable to assign the regiochemistry of bromine azide addition. However, the isolation of a small amount of  $\beta$ -bromostyrene, most likely formed by elimination of azido trimethylsilane, as a decomposition product of the intermediate azide on silica, together with NMR evidence, confirms the structural assignment.

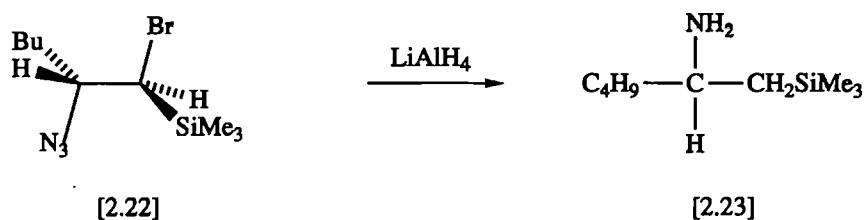
#### 2.2.2.2 Synthesis of other silylbromoazide adducts

Several other alkenes were examined during the course of this study all of which were found to form adducts with bromine azide. Most of these led to the formation of silylaziridines on reduction.

*Trans*-1-trimethylsilylhexene also forms an adduct with bromine azide but only by the *N*-bromosuccinimide route. Triphenylvinylsilane, and divinyl dimethylsilane form adducts via the other route.

With *trans*-1-trimethylsilylhexene the bromine/sodium azide route failed to give a silylbromoazide, whereas the *N*-bromosuccinimide route gave the corresponding bromoazide adduct [2.22] in good yield (71%). The failure of the former route could be attributed to the inability of the butyl group to stabilize an intermediate open chain carbocation. Whereas formation of the cyclic bromonium ion may still be viable, the azide ion is too weakly nucleophilic in such a medium to effect ring opening, so no bromoazide adduct would be formed.

A number of difficulties were encountered in finding a suitable method for reducing [2.22] to the corresponding silylaziridine. Several methods were attempted and these include reactions with lithium aluminium hydride, K-selectride, sodium borohydride, calcium hydride, and triphenylphosphine as well as a catalytic hydrogenation method. When lithium aluminium hydride was used as the reducing agent, 2-amino-1-trimethylsilylhexane, [2.23] was obtained in quantitative yield (Equation 2.1).

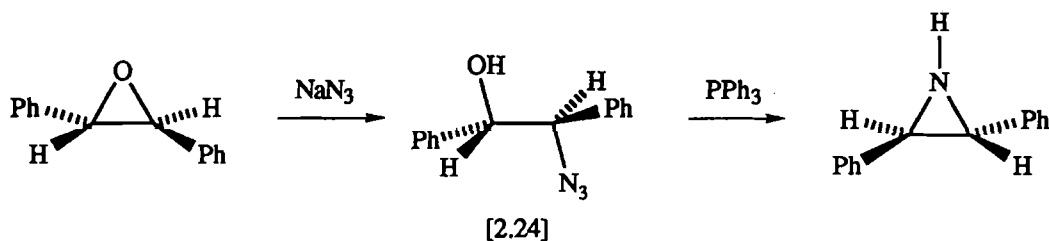


Equation 2.1

The regiochemistry of this product can be assigned on the basis of proton NMR spectroscopy. A doublet of doublets (2 protons) at 0.68 ppm corresponds to the two protons on the carbon adjacent to silicon. The proton on the carbon adjacent to nitrogen resonates as a multiplet. The other possible regioisomeric product (1-trimethylsilyl-1-aminohexane), should give rise to a pair of doublets of triplets (ignoring geminal coupling) which is not observed. Since the bromo function is lost, it is likely that the amine is formed by further reduction of a cyclized product.

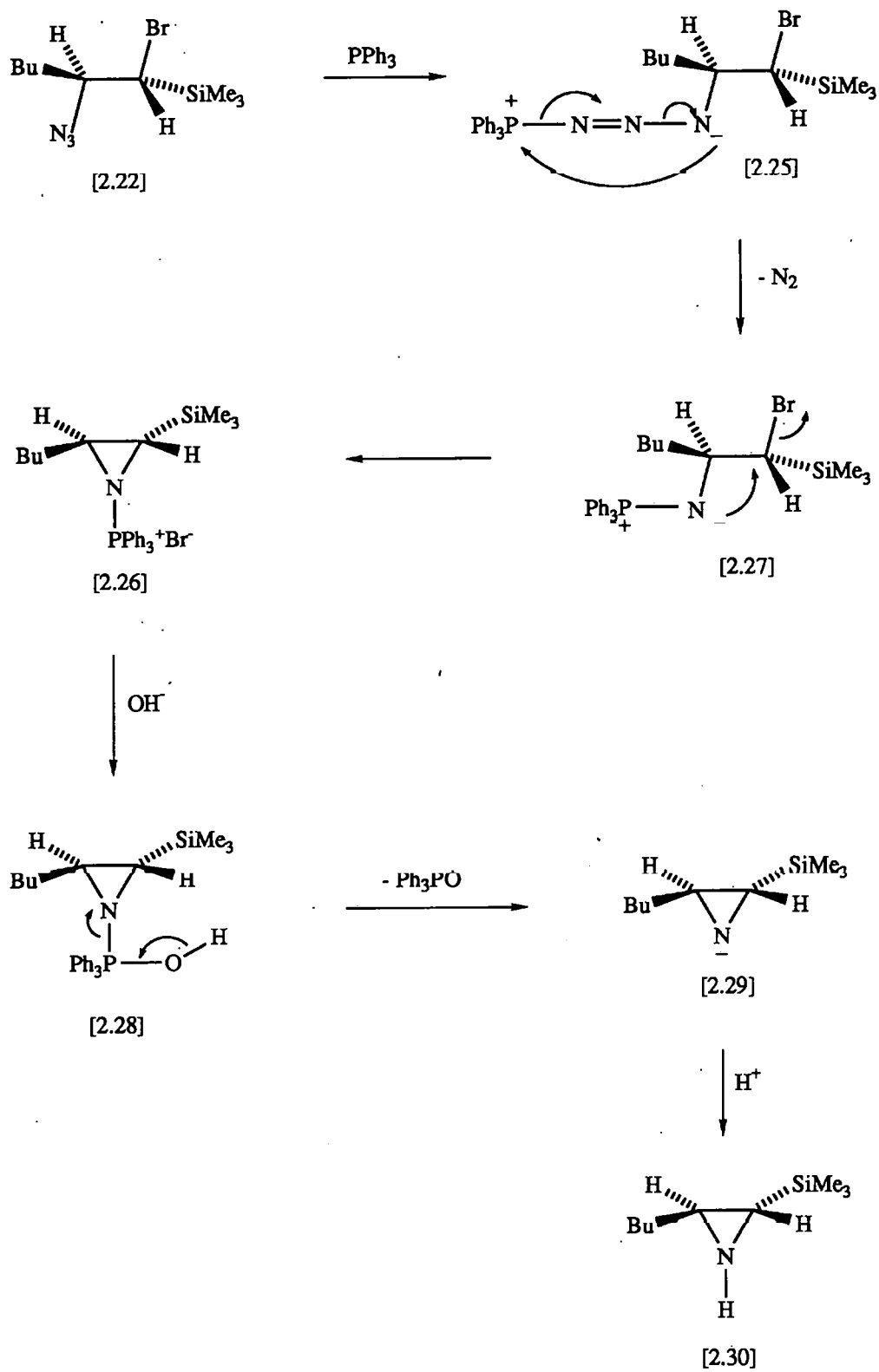


While the possibility of bromide hydrogenolysis prior to azide reduction cannot be discounted, it is unlikely in view of the sensitivity to steric effects of such reactions<sup>13</sup>. The bulky trimethylsilyl group severely hinders the approach of the nucleophilic hydride complex. A reaction involving inverse addition of a lithium aluminium hydride slurry to the azide (in the hope that the aziridine could be isolated when the reducing agent was not in excess) still led to the formation of the fully reduced product. However, the clean reaction with [2.22] prompted us to look for a more selective reducing agent for this compound in the form of K-selectride. In this case the reaction was carried out in THF at a range of temperatures from - 78 °C to room temperature, the reducing agent being added slowly to a stirred solution of [2.22] followed by an aqueous ammonium chloride work-up. In each case the product mixture obtained was consistent with an aziridine or aziridinium species with a tri(*s*-butyl)boron group coordinated to the nitrogen. In an attempt to isolate the free aziridine other work-up procedures were also used. These included hydrolysis with sodium bicarbonate and purging with ammonia gas followed by aqueous work-up. Purification proved impossible and so the procedure was abandoned. When sodium borohydride or calcium hydride was used as the reducing agent, the starting  $\beta$ -bromoazide was recovered unreacted. Another procedure which was pursued, in the hope of obtaining the  $\beta$ -bromoamine, which might subsequently undergo reductive cyclization, was catalytic hydrogenation. A broad range of conditions were tried, varying the solvent, the catalyst and the means of introducing the hydrogen. The reactions were followed by tlc and NMR spectroscopy, but with most no reaction whatever was observed. However, a reaction carried out in ethanol using 10% by weight of a 5% palladium on carbon catalyst led to elimination of trimethylsilyl azide. Finally a method was developed for the successful reduction of the azide to the corresponding aziridine, *trans*-3-butyl-2-trimethylsilylaziridine. This reaction involved heating a mixture of triphenylphosphine and the azide in THF at 50 °C for 1.5 hours with subsequent addition of sodium hydroxide solution and acidic work-up<sup>20</sup>. A similar method had been used previously in the synthesis of aziridines from  $\beta$ -azido alcohols<sup>21</sup> e.g., [2.24] (scheme 2.14).



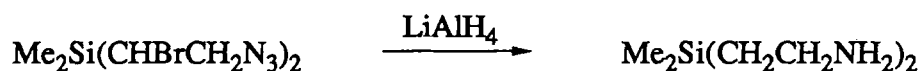
Scheme 2.14

A plausible mechanism for the reaction with our silylbromoazide, [2.22] is outlined in Scheme 2.15. In the first step triphenylphosphine adds by electrophilic attack on the terminal nitrogen atom of the azide function to give [2.25].  $N_2$  is then eliminated, and cyclization of the resultant ylide, [2.27] occurs by intramolecular nucleophilic substitution, leading to an aziridinyl phosphonium bromide, [2.26]. Alkaline work-up leads to elimination of triphenylphosphine oxide from [2.28] and subsequent protonation of the intermediate, [2.29] yields the product aziridine, [2.30]. That the product obtained in this reaction was actually the *trans* aziridine shown, was confirmed by comparison with NMR spectra of an authentic sample. This was possible since a new route to this compound was subsequently developed by lithium aluminium hydride reduction of the *N*-carboethoxyaziridine [2.32], (section 2.2.4). That the *trans* isomer was obtained was established by the NMR coupling constant of the ring protons ( $J = 4.6$  Hz).



**Scheme 2.15**

With the triphenylsilylalkene, the other route using bromine azide prepared in dichloromethane from sodium azide and bromine, proved to be the most successful. Here longer reaction times were required as well as an increased proportion of sodium azide in order to avoid production of the dibromo adduct. Silylaziridines were formed in good yield on reduction with lithium aluminium hydride, 88% in the case of 2-triphenylsilylaziridine. In the case of divinyl dimethylsilane a bromoazide adduct was identified but it decomposed rapidly, especially in light. An attempt was made to reduce this compound with lithium aluminium hydride and the major product obtained had spectra consistent with dimethyl di(2-aminoethyl)silane, (Equation 2.2).



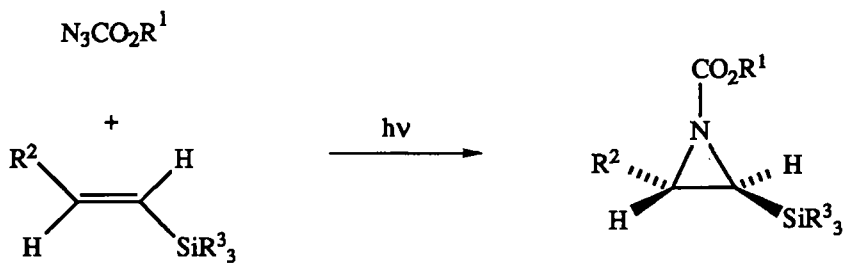
Equation 2.2

The course of this reaction may be similar to that followed by the butyl substituted aziridine described above. That is, the product may have been formed by ring opening of an intermediate aziridinyl compound by hydride ion although there was no evidence for such a compound from NMR spectra. There is no apparent reason for the differences in reactivities of these compounds.

### 2.2.3 Synthesis of silylaziridines by the photochemical decomposition of alkyl azidoformates in the presence of vinylsilanes.

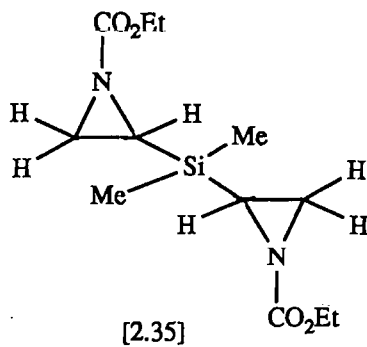
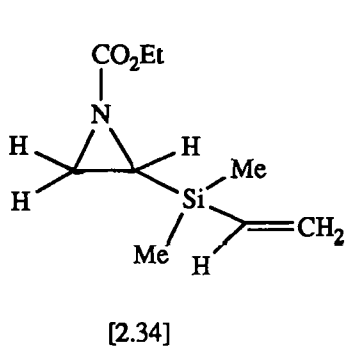
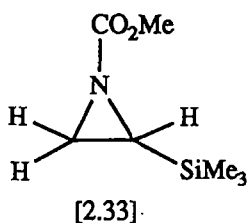
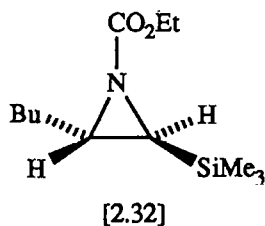
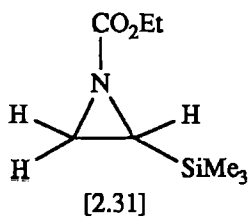
Aziridines may be synthesized by the reaction between nitrenes and alkenes<sup>22</sup>. The most common reaction of this type involves the use of acyl azides, in particular, alkyl azidoformates. The nitrene intermediate for the reaction may be generated thermally or photochemically. The method we developed in this current work involved the use of

photochemically generated nitrenes from two acyl azide precursors, ethyl and methylazidoformate (Equation 2.3).



### Equation 2.3

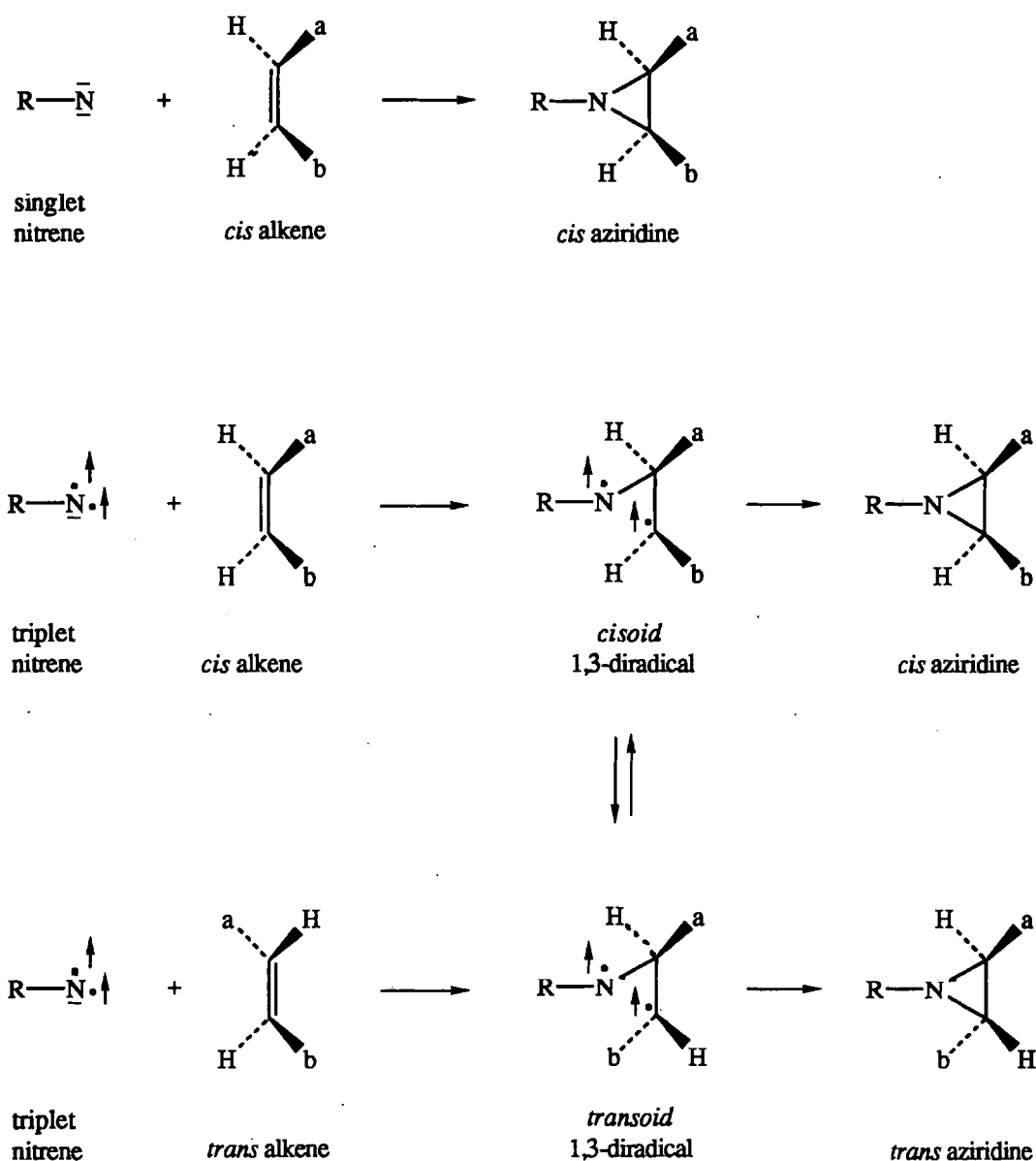
These were found to add to a number of functionalized vinylsilanes to give a wide variety of new silylaziridines, a selection of these are shown below.



The reactions were carried out in the absence of solvent and were generally complete within two to four days. The silylaziridines were formed in good yield and were purified by column chromatography. The reactions were fairly clean although there was a small amount of a by-product present in most of the product mixtures which is thought to have resulted from (formal) nitrene dimerization.

The most facile and high yielding reaction was that between ethyl azidoformate and vinyltrimethylsilane. The product of this reaction had already been synthesized by Lukevics<sup>23</sup>, however, our procedure represents a much more facile and cleaner reaction. In the current work, when substituted vinylsilanes were used, the configuration of the alkene was retained in the product.

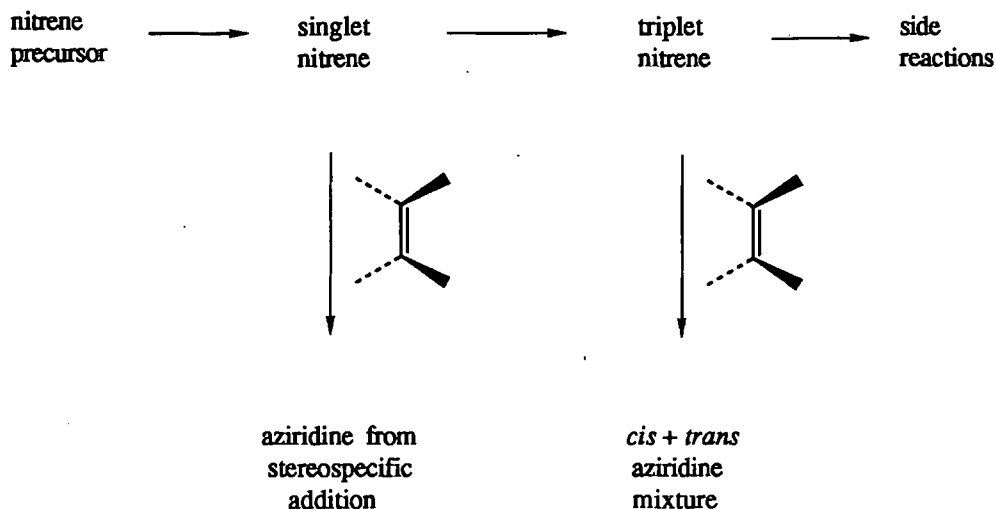
Azidoformates may yield nitrenes by thermal or photochemical means. The thermal decomposition reaction however often occurs at temperatures greater than is required for rapid 1,3-dipolar cycloaddition of the azide to alkenes to yield triazolines. The formation and subsequent decomposition of triazolines has been discussed in Chapter 1. It is difficult to distinguish between a triazoline and a nitrene mechanism. By a thermal route, the formation and subsequent decomposition of a triazoline might be indicated by an enhanced rate of nitrogen evolution. However for a photolytic azide decomposition, the rate of nitrogen evolution depends on the light flux and the quantum yield. Whilst reactions which proceed via a triazoline intermediate are in general stereospecific (the geometry of the starting alkene being retained in the aziridine product), the same reactions involving nitrenes may give rise to a mixture of *cis* and *trans* aziridines depending on the conditions used. The stereochemistry observed is dependent on whether the nitrene is in the singlet or triplet state<sup>24</sup>. Both singlet and triplet nitrenes are capable of adding to alkenes. With singlet nitrenes addition takes place in a single step and the reaction is stereospecific. Triplet nitrenes however, add by a two-step mechanism via a triplet 1,3-diradical as shown in Scheme 2.16.



**Scheme 2.16**

Generally, the nitrene is generated in the singlet state and the triplet nitrene may arise from intersystem crossing if sufficient time elapses before an alkene molecule is encountered in a reactive collision. This latter situation may arise when the reaction is carried out in dilute solution and has been studied by Lwowski for ethoxycarbonylnitrene (generated from ethyl azidoformate)<sup>25</sup>. When the concentration of alkene is low, the number of collisions between alkene and nitrene per unit time is low. Thus a larger fraction of singlet nitrene will be converted to the triplet ground state which reacts non-stereospecifically with the

alkene resulting in a mixture of *cis* and *trans* aziridines in the product mixture<sup>26</sup>. This idea is represented in Scheme 2.17.



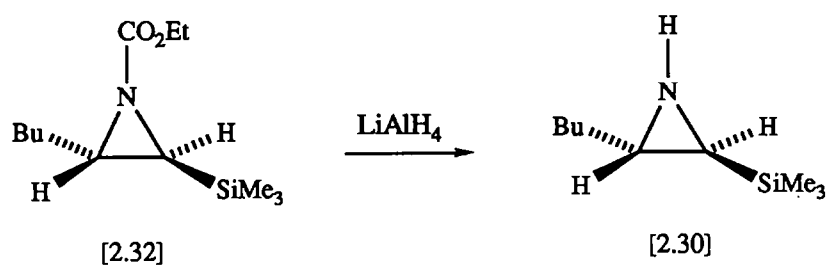
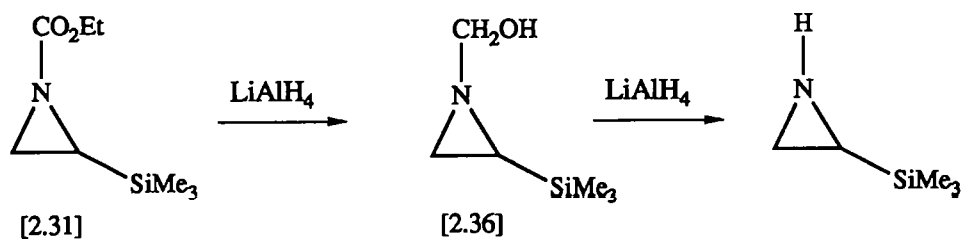
Scheme 2.17

In practice the alkene concentration will always be such as to allow some of the nitrene to convert to the triplet state. The situation becomes more complicated when a photolysis route is used to generate the nitrene from ethyl azidoformate. Here one third of the nitrene may be generated directly in the triplet state. However, in the current work, there was no evidence by NMR for the presence of a *cis* aziridine when a *trans* substituted alkene (*trans*-1-trimethylsilylhex-1-ene) was used.

#### 2.2.4 Silylaziridines formed by ring preserving reactions of parent silylaziridines

Two silylaziridines were formed by the reaction of lithium aluminium hydride with 1-carboethoxy-2-trimethylsilylaziridine [2.31] and *trans*-3-butyl-1-carboethoxy-2-trimethylsilylaziridine, [2.32] leading to 1-hydroxymethyl-2-trimethylsilylaziridine, [2.36] and *trans*-3-butyl-2-trimethylsilylaziridine [2.30] respectively (Scheme 2.18). This reaction is discussed in detail in Chapter 3.





**Scheme 2.18**

## 2.3 References

1. A.R. Bassindale, A.G. Brook, P.F. Jones and J.A.G. Stewart, *J. Organomet. Chem.*, **152**, C 25-28, (1978).
2. P. Zanirato, *J. Chem. Soc., Perkin Trans 1*, 2789, (1991).
3. F. Duboudin and O. Laporte, *J. Organomet. Chem.*, **156**, C 25-28, (1978).
4. F. Duboudin and O. Laporte, *J. Organomet. Chem.*, **174**, C 18-20, (1979).
5. E.J. Thomas and G.H. Whitham, *J. Chem. Soc., Chem. Commun.*, 212, (1979).
6. E.J. Grayson and G.H. Whitham, *Tetrahedron*, **44**, 4087, (1988).
7. E. Lukevics, V.V. Dirrens, Y.S. Goldberg, E.E. Liepinsh, I.Y. Kalvinsh, and M.V. Shymanska, *J. Organomet. Chem.*, **268**, C 29-32, (1984).
8. R.S. Atkinson, and B.J. Kelly, *J. Chem. Soc., Chem. Commun.*, 836, (1989).
9. M.C.C. Soobramanien, Ph.D. Thesis, The Open University, Milton Keynes, (1988).
10. G.E. Ham, *J. Org. Chem.*, **29**, 3052, (1964).
11. E. Lukevics in "Frontiers of Organosilicon Chemistry", Ed. A.R. Bassindale and P.P. Gaspar, The Royal Society of Chemistry, Cambridge, 1991, p. 383.
12. F.W. Fowler, A. Hassner and L.A. Levy, *J. Am. Chem. Soc.*, **89**, 2077, (1967).
13. A. Hassner, G.J. Matthews and F.W. Fowler, *J. Am. Chem. Soc.*, **91**, 5046, (1969).
14. D. Van Ende and A. Krief, *Angew. Chem. Internat. Edit.*, **13**, 279, (1974).
15. A. Hassner and F. Boerwinkle, *J. Am. Chem. Soc.*, **90**, 216, (1968).
16. R.C. Cambie, R.C. Hayward, P.S. Rutledge, T. Smith-Palmer, B.E. Swedlund and P.D. Woodgate, *J. Chem. Soc., Perkin 1*, 180, (1977).
17. A. Hassner, *Accounts Chem. Res.*, **4**, 9, (1971).
18. T.H. Chan and K. Koumaglo, *Tetrahedron Lett.*, **27**, 883, (1986).
19. A.R. Bassindale and P.G. Taylor, in "The Chemistry of Organic Silicon Compounds", Ed. S. Patai and Z. Rappoport, Wiley, New York, 1989.

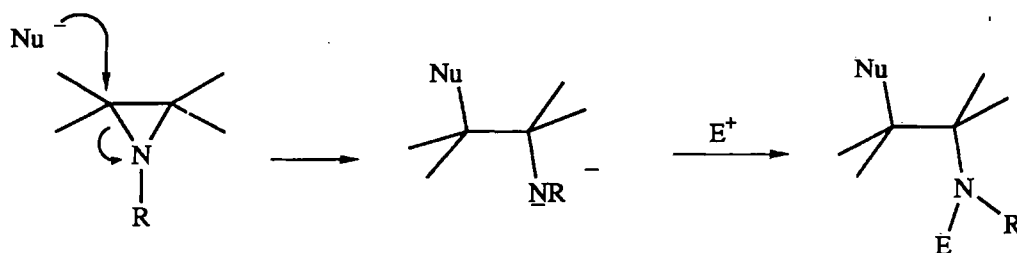
20. S. Murahashi, Y. Tanigawa, Y. Imada and Y. Taniguchi, *Tetrahedron Lett.*, **227**, (1986).
21. Y. Ittah, Y. Sasson, I. Shahak, S. Tsaroom and J. Blum, *J. Org. Chem.*, **43**, 4271, (1978).
22. T.L. Gilchrist and C.W. Rees, "Carbenes Nitrenes and Arynes", Nelson, 1969, Chapter 7.
23. E. Lukevics, V.V. Dirrens, Y.S. Goldberg, E.E. Liepinsh, M.P. Gavars, I.Y. Kalvinsh, and M.V. Shymanska, *Organometallics*, **4**, 1648, (1985).
24. W. Lwowski and J.S. McConaghy, Jr., *J. Am. Chem. Soc.*, **87**, 5490, (1965).
25. W. Lwowski and F.P. Woerner, *J. Am. Chem. Soc.*, **87**, 5491, (1965).
26. J.S. McConaghy, Jr., and W. Lwowski, *J. Am. Chem. Soc.*, **89**, 4450, (1967).

# REACTIVITY OF SILYLAZIRIDINES

## 3.1 Introduction

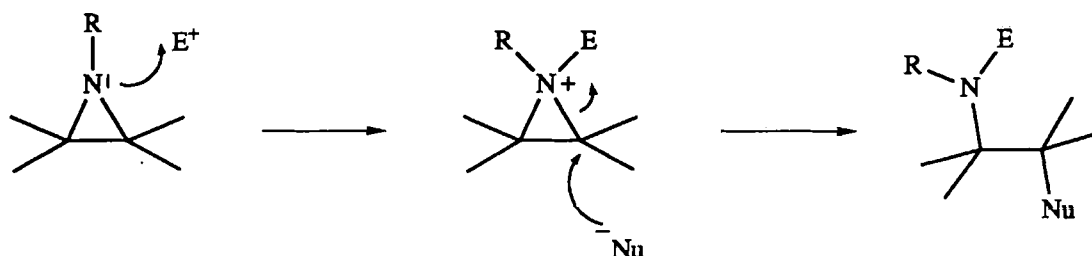
Small ring heterocycles such as epoxides and aziridines are highly susceptible to ring opening reactions. This is due in part to ring strain and also to the polarizing effect of the heteroatom. The ease with which ring cleavage occurs depends on the steric effects and electronic influence of the substituents on carbon, and also on the nature of the attacking reagents. In the case of aziridines, the ease of ring opening will also be dependent on the nature of substituents on nitrogen, strong electron withdrawing groups facilitate the nucleophilic ring opening reaction.

Ring opening reactions may occur by direct nucleophilic attack as shown in Scheme 3.1,



Scheme 3.1 nucleophilic ring opening of an aziridine

or by electrophilic attack of the reagent on nitrogen to form an intermediate aziridinium salt which is subsequently attacked by the corresponding anion (Scheme 3.2). Nucleophilic ring opening reactions of aziridines are therefore often subject to acid catalysis.



**Scheme 3.2** electrophilic ring opening of an aziridine

Aziridines are capable of undergoing ring preserving reactions such as protonation or alkylation on nitrogen, fragmentation reactions, and reactions on substituents. However, the vast majority of the reactions attempted during the course of this study gave products of ring cleavage. Desilylation of aziridines, with preservation of the ring structure has been studied in detail and the results are reported in Chapter 4 of this thesis. One of the reactions carried out led to the isolation of an aziridinium salt, without subsequent ring cleavage. Also, in a few cases, reaction occurred solely at the substituent on nitrogen and these are reported here.

Most of the aziridines synthesized during the course of this study were subjected to reaction with electrophilic reagents, leading to products of ring cleavage. Some of the ring opened products underwent rearrangement with the formation of enamines. Surprisingly, all of the aziridines studied failed to react with any nucleophilic agents, and this is discussed in section 3.7.

Such a study as this involves potentially many reactions, however, it was not possible to carry out a completely exhaustive examination. The aim of this study was to obtain some knowledge about the scope and range of reactions of silylaziridines - an area which has not been studied in detail to date. Consequently, some reactions were studied briefly and no attempt was made to optimise all reactions or identify products in 'complex', mixtures. Silylaziridines should represent highly useful precursors in organic synthesis since they can be prepared stereoselectively, and the geometry of the ring is preserved during reactions.

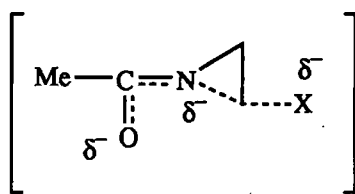
To begin with, in section 3.2, some general aspects of aziridine ring cleavage with nucleophilic reagents and electrophilic reagents is described. Then, the specific case of silylaziridine ring cleavage is discussed, explaining the rationale for choosing the silylaziridines synthesized for this study. The reactions examined showed a fairly general trend, most leading to products of ring cleavage. Where ring opening did occur, there was substantial evidence that  $\alpha$ -opening occurred exclusively. The general aspects of this type of reaction are discussed in detail in section 3.3 for the reactions involving hydrogen halides, but the mechanistic considerations in this case can be applied to most of the other ring opening reactions. These are, the reactions with triflates such as trifluoromethanesulphonic acid and methyl trifluoromethanesulphonic acid (section 3.4), trifluoroacetic acid (section 3.5) and trimethylsilylhalides (section 3.6). Nucleophilic ring opening reactions were unsuccessful and since this observation is in itself significant, a section (3.7) on this subject has been included. Aziridines which are activated to nucleophilic ring opening owing to the effect of substituents on the nitrogen atom, may often suffer from competition between ring opening and reaction on the substituent. Indeed, in the current work, one nucleophilic ring opening reaction which was attempted, resulted in complete reaction at the substituent, and this is discussed in section 3.7.3.

## 3.2 Reactions involving ring cleavage - preliminary considerations

### 3.2.1 Ring opening of aziridines with nucleophilic reagents

Whereas epoxides undergo nucleophilic ring opening with relative ease, aziridines undergo direct attack only when the nitrogen atom bears a strong electron accepting group (tosyl, acyl, cyano etc.). In the case of simple basic aziridines (hydrogen or alkyl group on nitrogen) acid catalysis is essential except where very powerful nucleophiles like the anions of amines or phosphines are employed. Indeed, even with such strong nucleophiles, forcing conditions may be required (up to 120 °C for 3 weeks in some cases<sup>1</sup>). However,

Ham<sup>2</sup> has coined the expression 'activated aziridine' to encompass those which possess substituents on nitrogen capable of stabilizing a negative charge in an aziridine-nucleophile transition state (such as [3.1]).



[3.1]

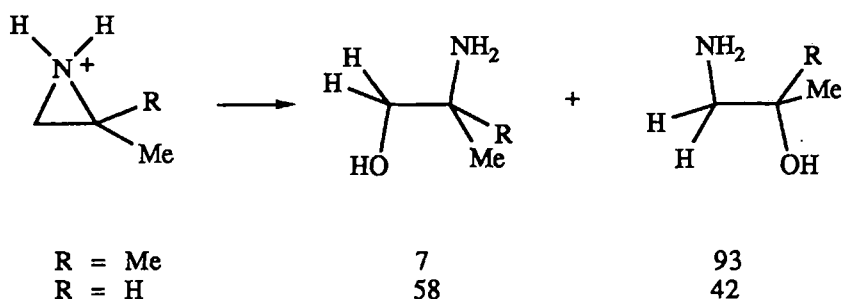
Other aziridines, which do not contain such a group were referred to as 'basic' aziridines, e.g., ethyleneimine. Aziridines which do possess an activating substituent on nitrogen readily undergo ring opening with nucleophiles, even in the absence of acid catalysis, which is normally a pre-requisite.

Ring opening reactions of aziridines by nucleophilic reagents has been shown to proceed with inversion of configuration at the point of attack<sup>1</sup>. With unsymmetrical aziridines the nucleophile attacks at the less hindered carbon atom so that ring opening in one direction is predominant<sup>3</sup>. The mechanistic aspects of such reactions will be discussed in section 3.7.

### 3.2.2 Ring opening of aziridines with electrophilic reagents

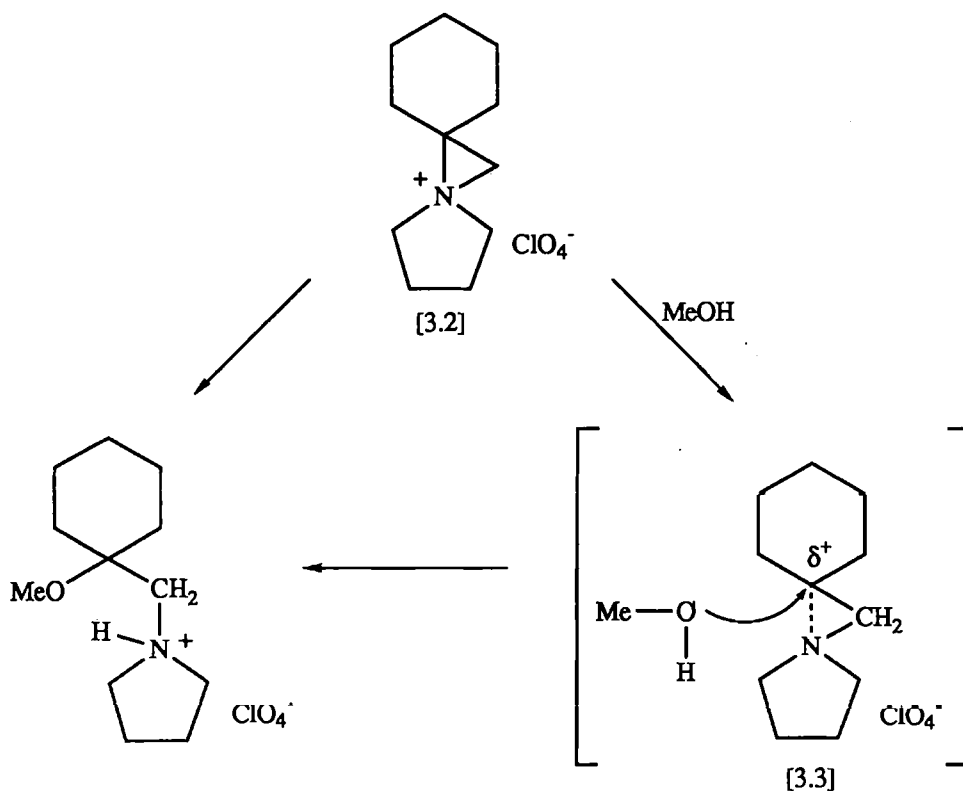
Aziridines (and epoxides) are more susceptible to ring opening than cyclopropane, not only because of the polarity effect of the heteroatom, but also because of their ability to coordinate with electrophiles to generate a charged intermediate. The so-formed protonated aziridines or aziridinium salts are extremely susceptible to attack by nucleophiles, and their isolation is only feasible when anions of low nucleophilicity are employed. Attack on the ring carbon atoms proceeds stereospecifically with inversion of configuration. Usually the regiochemistry is determined by steric factors so that attack at the less substituted ring carbon is predominant. This is known as 'normal' ring cleavage. However, when an

electron releasing substituent is attached to one of the carbon atoms the opposite regiochemistry ('abnormal' ring cleavage) prevails owing to stabilization of positive charge development in the corresponding transition state.



**Equation 3.1** product ratios in the hydrolysis of aziridines

Here bond breaking becomes more important than bond making, and a more  $S_N1$ -like mechanism may prevail. This situation arises when the aziridine contains a dialkyl substituent on one of the carbon atoms as exemplified in Equation 3.1, the acid-catalysed hydrolysis of 2,2-dimethylaziridine<sup>4</sup>.



**Scheme 3.3**



Under acid conditions, or with aziridinium salts, electronic factors are more important than steric influences. With very nucleophilic attacking species, ring opening occurs by an  $S_N2$  mechanism. With poorer nucleophiles a more  $S_N1$ -like mechanism may predominate, as shown in Scheme 3.3<sup>5</sup>. Ring cleavage of [3.2] is such as to yield the most stable carbonium ion, [3.3] which subsequently reacts with the nucleophile.

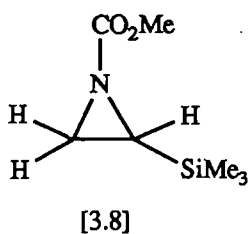
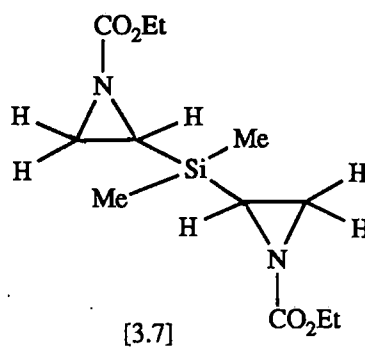
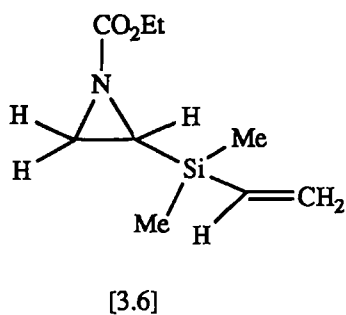
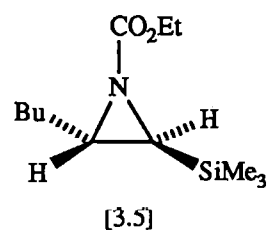
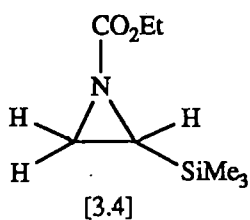
### 3.2.3 Ring opening reactions of 2-silyl substituted aziridines and epoxides

The ring opening reactions of silyl substituted epoxides is well documented in the literature. Silylaziridines on the other hand have received much less attention. In general, the reactions proceed to give predominantly products of  $\alpha$ -cleavage. In view of the well known stability of cations  $\beta$  to silicon, it might be expected that an  $S_N1$ -type transition state (leading to  $\beta$ -cleavage) would be a highly stabilized arrangement. However, the relative orientations of the C-Si bond and the incipient positive charge are such that hyperconjugative overlap is minimal. The consistently observed high regioselectivity suggests that the silyl group facilitates bimolecular nucleophilic displacement  $\alpha$  to silicon. This is due to the ability of silicon to stabilize negative charge build up on the  $\alpha$ -carbon in the transition state for the  $S_N2$  reaction<sup>6,7</sup>.

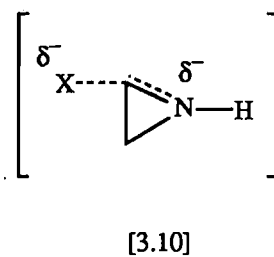
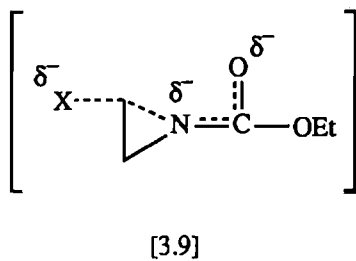
In the light of previous work, it was decided to synthesize an activated aziridine, in order to enhance the susceptibility towards ring opening, in particular nucleophilic ring opening<sup>8</sup>. For these reasons, silylaziridines having an *N*-carboalkoxy substituent were synthesized. A selection is shown below. A broad series of reactions was carried out using 1-carboethoxy-2-trimethylsilylaziridine, [3.4] and only a few reactions with the other aziridines shown, which did not yield clean products.

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<sup>8</sup> It was also thought that such aziridines would exhibit an enhanced propensity towards desilylation.



In this case the ability of the carboalkoxy substituent to conjugate with the partial negative charge on nitrogen in the transition state, [3.9] greatly reduces the activation energy required to attain this state compared with that for a more basic aziridine such as ethyleneimine [3.10].



This ability of the *N*-carboethoxy substituent to activate such aziridines towards nucleophilic attack is well known<sup>2,8,9</sup>. The effect is greatest for purely nucleophilic reactions, however, no nucleophilic ring opening reactions studied here were successful. In the case of reactions with electrophilic agents, the dominant effect is inductive withdrawal. The electrophile associates with the nitrogen atom and the positive charge on the nitrogen results in polarisation of the C-N bond. The electron deficient carbon atom is then susceptible to nucleophilic attack. In the case of a silylated, *N*-carboethoxy substituted aziridine, although the substituent may promote the ring opening reaction, the direction of ring opening is controlled by the silicon.

#### 3.2.4 Spectroscopic evidence for the direction of ring opening

There is a substantial amount of spectroscopic evidence which suggests that ring opening occurs (exclusively) at the carbon  $\alpha$  to silicon. In most cases the combined evidence leaves little doubt as to the mode of ring opening (i.e.,  $\alpha$ - or  $\beta$ -). However, there are one or two examples where although the evidence is fairly strong, it is not conclusive.

The  $^{13}\text{C}$  NMR data are shown in Table 3.1. The following observations can be made.

1. Some experiments on ring opening of silylaziridines carried out by Soobramanien have been shown to proceed by  $\alpha$ -attack (entries 13-18). In these cases the shift of  $\text{CXR}^4\text{Si}$  correlates closely with our value for the same attacking species, e.g., entries 1, 9, 10, 13 and 15 for chloride; and 8 and 18 for hydroxide.
2. For aziridine *a*, (entries 1-8) the chemical shift of  $\text{CXR}^4\text{Si}$  varies according to the attacking nucleophile.
3. Where an iodide nucleophile was used (entries 4 and 11), a heavy atom effect was observed, i.e., the carbon attached to the iodine atoms had a low chemical shift.
4. For a particular aziridine, where the nucleophilic species is the same (but the electrophilic partner differs e.g., HBr and TMSBr, entries 2 and 3, or HOTf and

**Table 3.1**  $^{13}\text{C}$  NMR shifts of former ring carbons in ring opened species

Entry	Aziridine	Reagent	$\text{CR}^2\text{R}^3$	$\text{CXR}^4\text{Si}$
1	<i>a</i>	HCl	44.3	51.4
2	<i>a</i>	HBr	40.0	43.5
3	<i>a</i>	TMSBr	47.3	43.2
4	<i>a</i>	TMSI	47.4	21.8
5	<i>a</i>	$\text{CF}_3\text{CO}_2\text{H}$	41.7	74.2
6	<i>a</i>	HOTf	45.1	81.9
7	<i>a</i>	MeOTf	50.8	79.6
<sup>1</sup> 8	<i>a</i>	$\text{HClO}_3$	45.0	66.9
29	<i>b</i>	HCl	61.0	51.2
10	<i>c</i>	HCl	65.2	52.8
11	<i>d</i>	TMSI	50.9	22.3
12	<i>e</i>	$\text{CF}_3\text{CO}_2\text{H}$	35.9	73.4
<sup>2</sup> 13	<i>f</i>	HCl	66.9	50.5
<sup>2</sup> 14	<i>f</i>	HBr	67.0	42.6
<sup>2</sup> 15	<i>g</i>	HCl	73.6	49.4
16	<i>g</i>	HBr	58.3	52.3
<sup>2</sup> 17	<i>g</i>	HBr	74.4	41.2
<sup>1</sup> 18	<i>g</i>	$\text{CF}_3\text{CO}_2\text{H}$	67.4	66.1

*a* 1-carboethoxy-2-trimethylsilylaziridine, [3.4]

*b* *cis*-3-phenyl-2-trimethylsilylaziridine, [3.25]

*c* 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine, [3.29]

*d* 1-phenyl-2-trimethylsilylaziridine, [3.39]

*e* 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine, [3.20]

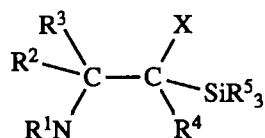
*f* *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine<sup>12</sup>

*g* *cis*-1,3-diphenyl-2-trimethylsilylaziridine<sup>12</sup>

<sup>1</sup>The nucleophilic species 'X' is OH.

<sup>2</sup>The hydrohalo acid adds twice.

The ring opened structure referred to is shown below.



MeOTf, entries 6 and 7, the chemical shift of  $\text{CXR}^4\text{Si}$  is very similar within each pair.

5. Where the same nucleophile attacks a different aziridine, the shift of one ring carbon remains fairly similar, whereas, the other differs e.g., entries 1,9,10, 13, and 15; 5 and 12; and 8 and 18.

### 3.3 Ring opening reactions of silylaziridines with hydrogen halides

#### 3.3.1 Introduction

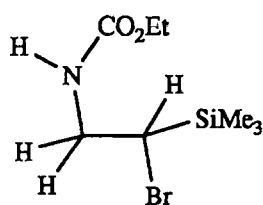
The reaction of gaseous hydrogen halides with most of the silylaziridines synthesized during the course of this work is reported in this thesis. Generally a deuteriochloroform solution of the aziridine was cooled to 0 °C, and the gaseous hydrogen halide was passed through the solution. The reactions were monitored by NMR spectroscopy. In most cases products of  $\alpha$ -ring cleavage were isolated in very good yield. In the case of the reactions of the *N*-phenyl,  $\alpha$ -carbomethoxyaziridines with hydrogen chloride, aniline hydrochloride was formed.

#### 3.3.2 Reaction of 1-carboethoxy silylaziridines with hydrogen halides

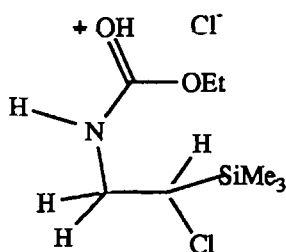
1-Carboethoxy-2-trimethylsilylaziridine reacts quantitatively with gaseous hydrogen halides to give the  $\alpha$ -ring opened  $\beta$ -haloamine products. The reaction proceeds with complete regioselectivity. That the bromine becomes attached to the  $\alpha$ -carbon is established by NMR data. Such reactions are known to proceed via an intermediate aziridinium salt. However, such a compound, although it is likely to be an intermediate, could not be detected owing to rapid ring cleavage. This ring opening of the protonated salts by the halide counter ion always occurs by  $\alpha$ -C-N cleavage. Since the halide becomes attached to the  $\alpha$ -carbon it is unlikely that an  $\text{S}_{\text{N}}1$  mechanism is involved, as this would lead to a transition state of higher energy compared to that for an  $\text{S}_{\text{N}}2$  reaction. This is because silicon can stabilize the incipient negative charge in a penta-coordinate transition

state. An  $S_N1$  mechanism would lead to an intermediate having a carbocationic site next to silicon, an arrangement which is destabilized to some extent<sup>10,11</sup>.

1-Carboethoxy-2-trimethylsilylaziridine was reacted with both hydrogen bromide and hydrogen chloride and, interestingly, different results were observed in each case. Both reactions lead to  $\alpha$ -ring opened products but with hydrogen chloride, addition took place twice leading to a protonated salt, [3.12]. Both compounds were stable at low temperatures and isolated in a pure form as white crystalline solids.

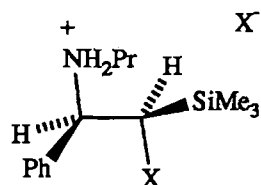


[3.11]



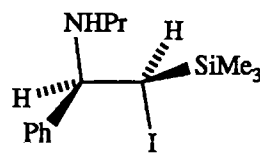
[3.12]

Previous work<sup>12</sup> on ring opening of *N*-alkyl and *N*-aryl silylaziridines with hydrogen halides has generated similar results. *Cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine gives the corresponding protonated salt, [3.13] with aqueous or gaseous hydrogen chloride or bromide and the  $\beta$ -haloamine, [3.14] with aqueous hydrogen iodide .



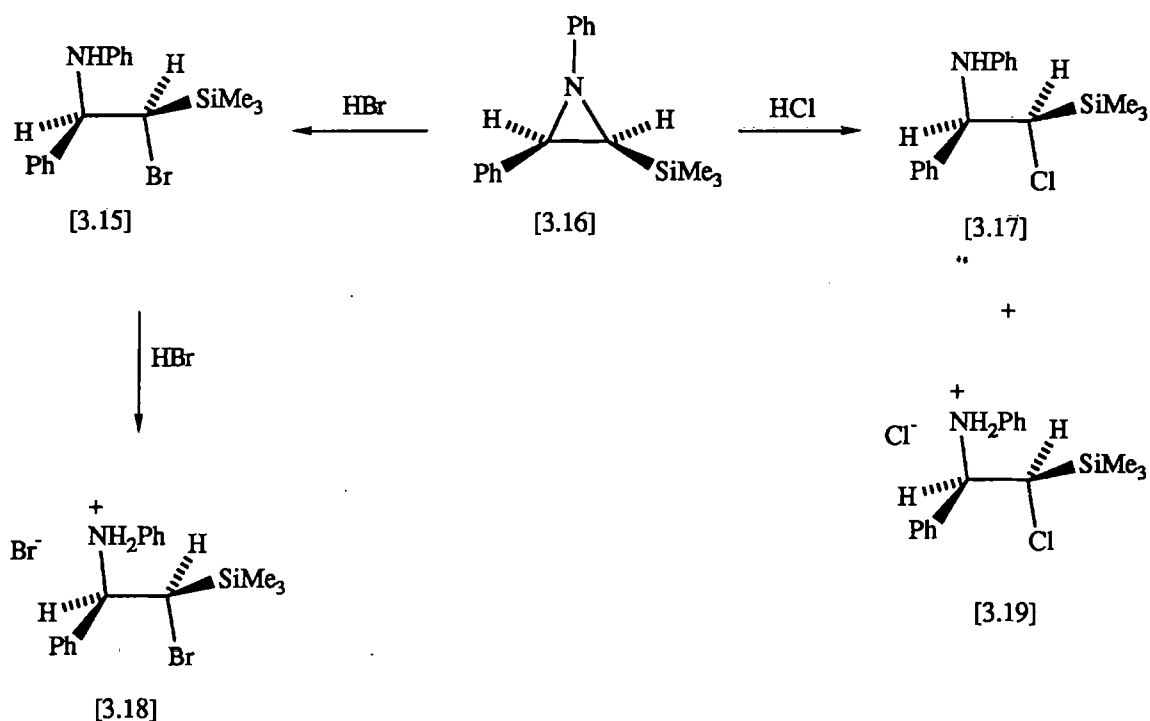
X = Cl, Br

[3.13]



[3.14]

When a less basic aziridine, *cis*-1,3-diphenyl-2-trimethylsilylaziridine, [3.16] was used, the results bear more similarity to the current work. With hydrogen bromide, only the unprotonated  $\beta$ -bromoamine, [3.15] was isolated, although it could be subsequently reacted further to give quantitatively the protonated salt [3.18] (Scheme 3.4).



Scheme 3.4

This is similar to the reaction of [3.4] when HBr was employed. When [3.16] was treated with hydrogen chloride the protonated salt, [3.19] was obtained in 38% yield, the

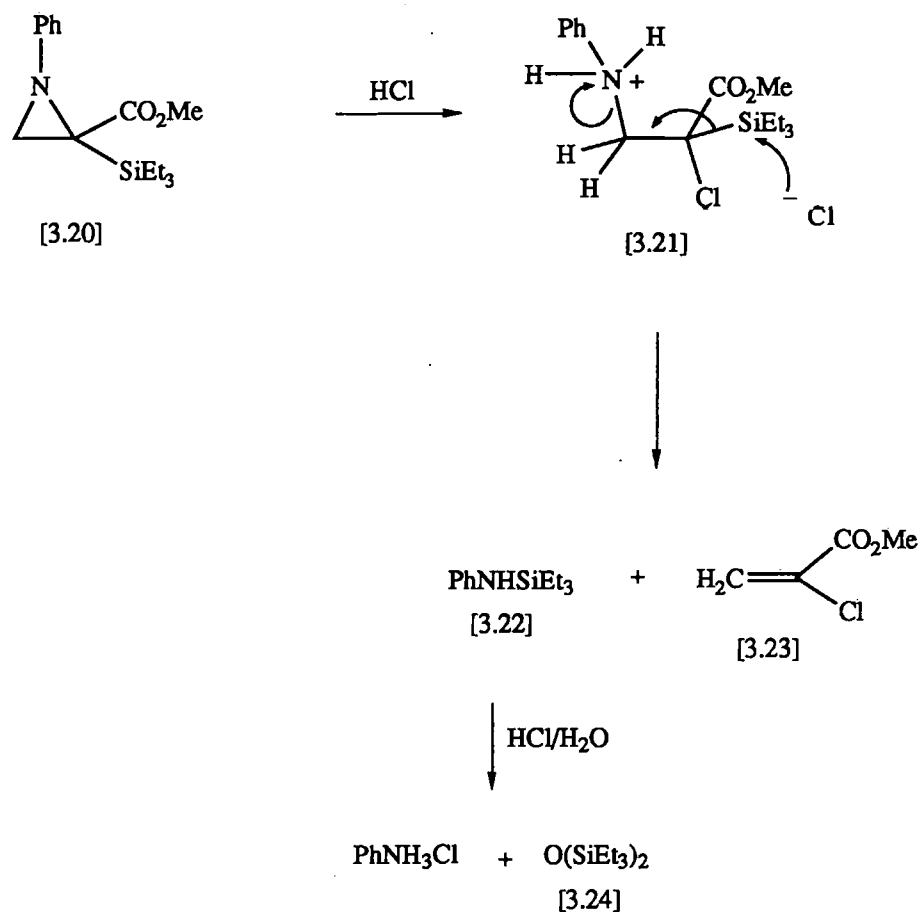
remainder being the  $\beta$ -chloroamine [3.17]. NMR data (coupled carbon-13 spectra) show that the reaction is completely regiospecific, the halide becoming attached to the  $\alpha$ -carbon.

In summary, all the silylaziridines examined consistently showed that acid catalysed ring opening occurs by  $\alpha$ -C-N cleavage, as has been observed in previous work on silylepoxides<sup>13-18</sup> and aziridines<sup>12</sup>.

### 3.3.3 Reaction of $\alpha$ -carbomethoxyaziridines with hydrogen halides

When the two  $\alpha$ -carbomethoxyaziridines, 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine, [3.20] and 2-carbomethoxy-2-dimethylsilyl-1-phenylaziridine, were treated with hydrogen chloride the only product that could be isolated in each case was aniline hydrochloride. Methyl 2-chloropropeneoate, [3.23], is volatile and would be lost on work-up, however, it is observed during the initial stages of the reaction in the proton NMR spectrum (doublet,  $J$  7.2 Hz, at 5.11 ppm). This would suggest that the  $\alpha$ -ring opened product is an intermediate in the reaction.



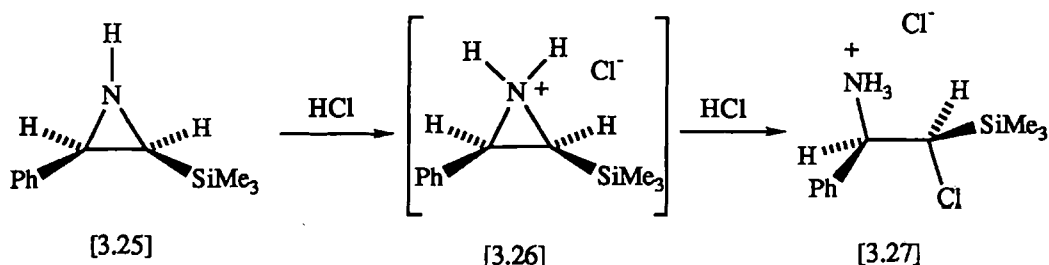


**Scheme 3.5**

It is possible that the aniline hydrochloride is formed by an aza-Peterson type elimination reaction and this is illustrated for [3.20] in Scheme 3.5. *N,N*-dimethylphenylsilylaniline or *N*-triethylsilylaniline [3.22], with an excess of hydrogen chloride in solution, on hydrolysis, give aniline hydrochloride and the corresponding siloxanes, in this case, [3.24].

### 3.3.4 Reaction of *N*-unsubstituted silylaziridines with hydrogen halides

*Cis*-3-phenyl-2-trimethylsilylaziridine [3.25] reacted with hydrogen chloride to give a ring opened protonated salt [3.27] (Scheme 3.6).



Scheme 3.6

As with the other silylaziridines it is expected that the first step in the reaction is protonation to give an intermediate aziridinium salt [3.26]. It was not possible to isolate the salt. However, its presence was observed in the proton NMR spectrum in the initial stages of the reaction. Again, ring opening occurs by  $\alpha$ -C-N cleavage. A similar result was obtained when *trans*-3-butyl-2-trimethylsilylaziridine was treated with hydrogen bromide. The mechanistic considerations discussed for the reaction of 1-carboethoxyaziridines with hydrogen halides are also valid in these two cases.

While the 1-carboethoxyaziridines ring open to give a  $\beta$ -halo carbamate, the unsubstituted aziridines ring open to give  $\beta$ -haloamines. The product containing the carbamate function will be only very weakly basic owing to conjugation of the nitrogen lone pair with the carbonyl group and it should therefore be less susceptible to further protonation. Conversely, the primary amino product will be fairly basic and should undergo rapid protonation to yield a protonated salt. Indeed this is the only product that is actually observed. Likewise, the work of Soobramanien<sup>12</sup> on ring opening of *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine with hydrogen halides gives similar results, as expected for a basic aziridine.

### 3.4 Ring opening reactions with triflates

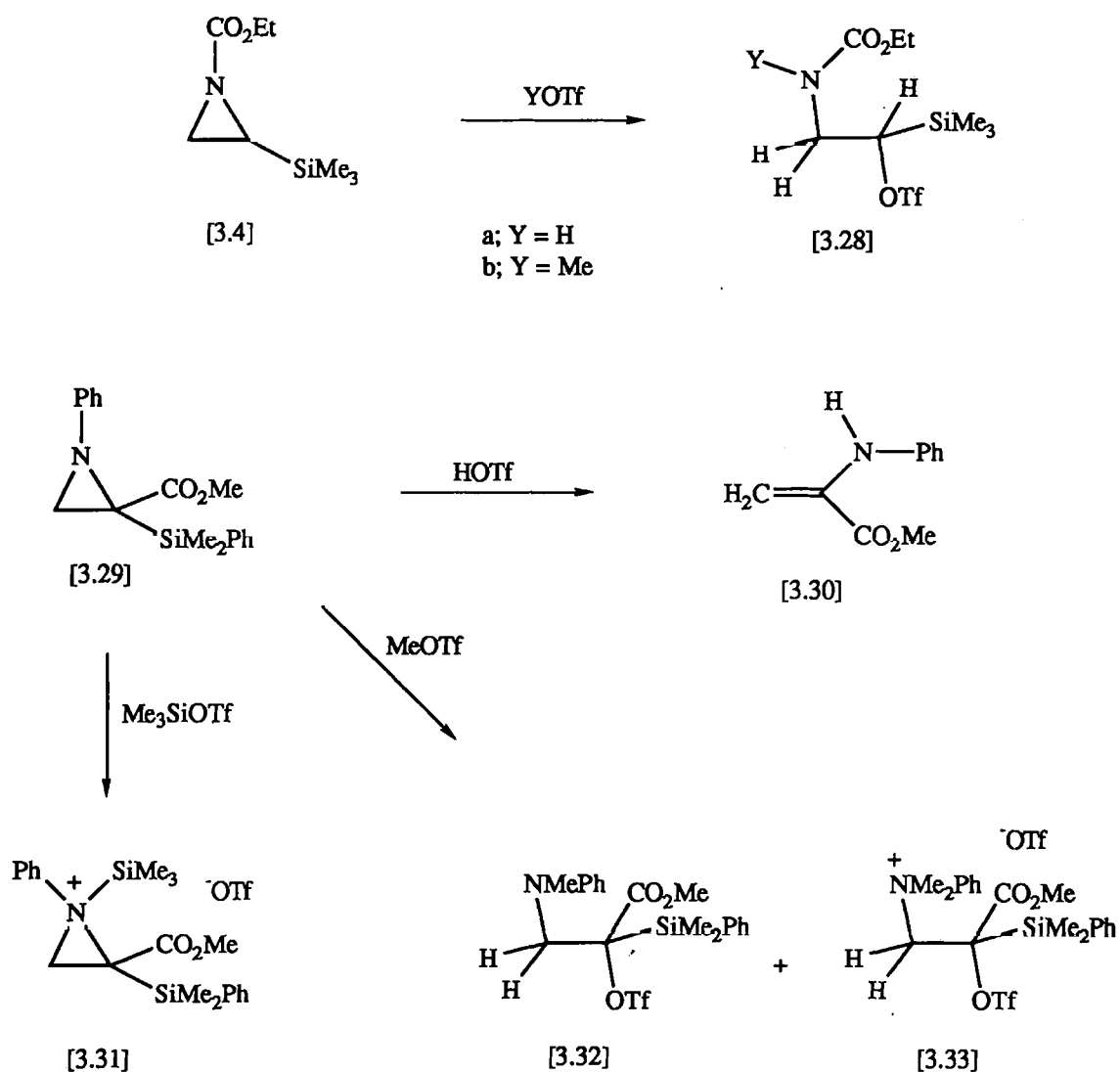
Trifluoromethanesulphonic acid, commonly known as triflic acid, is one of the strongest acids known, yet it is non-oxidising, and stable to heat and water<sup>19</sup>. Correspondingly the

triflate anion is an extremely weak nucleophile. It was thought therefore that triflates would readily protonate, alkylate or silylate an aziridine on the nitrogen atom, but possibly without ring destruction.

A series of reactions was carried out in which silylaziridines were reacted with triflic acid, methyl triflate or trimethylsilyl triflate. The reactions were followed by NMR spectroscopy and were carried out in a 5 mm NMR tube under nitrogen. The triflate was introduced via a syringe to a deuteriochloroform solution of the aziridine at -11 °C. In most cases, the reaction was complete within a few seconds.

With the 1-carboethoxyaziridine [3.4], a clean  $\alpha$  ring opening was observed with triflic acid or with methyl triflate to give [3.28a] and [3.28b] respectively. However, the  $\alpha$ -carbomethoxyaziridine [3.29] behaved differently, giving respectively, an enamine [3.30], ring cleavage products [3.32], and [3.33], and an aziridinium salt, [3.31] with triflic acid, methyl triflate and trimethylsilyl triflate.

All of the products however, were very unstable and decomposed within days or on exposure to air. No pure products could therefore be isolated, but NMR spectra confirm convincingly the structure of the adducts (Scheme 3.7).

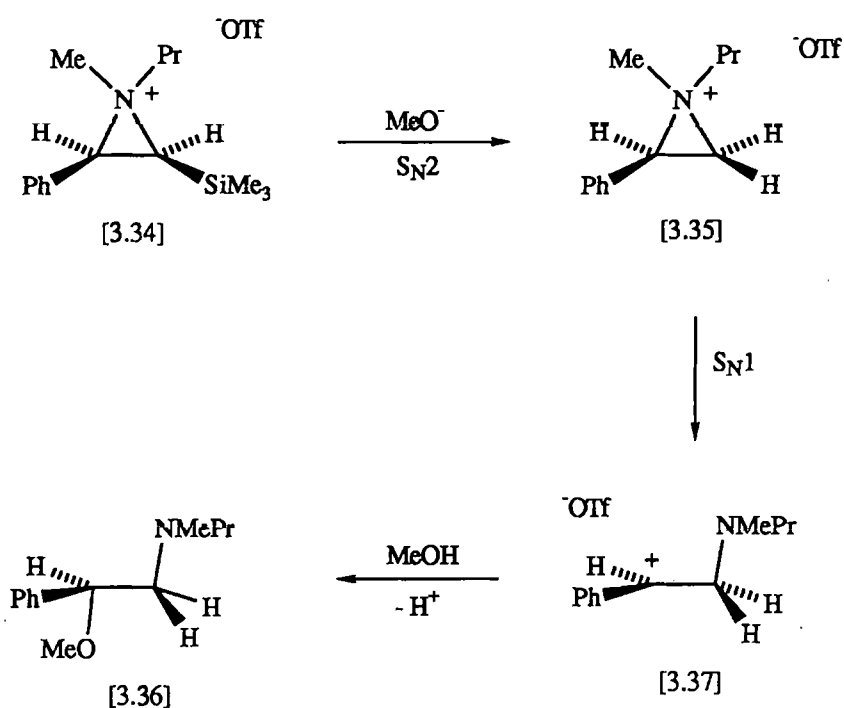


Scheme 3.7

Little work has been done on the reaction of silylaziridines with triflates. A stable quaternary salt, [3.34] has been isolated<sup>12</sup> from the reaction of *cis*-1-propyl-2-trimethylsilylaziridine with methyl triflate, whereas the same aziridine leads to a ring opened product with trifluoromethanesulphonic acid. The same study also included the reaction of methyl triflate with *trans*-1,3-diphenyl-2-trimethylsilylaziridine. This led to the quantitative production of trimethylsilyl triflate and another, unstable compound which could be neither isolated nor identified. While *cis*-3-phenyl-1-propyl-2-

trimethylsilylaziridine was methylated readily with methyl triflate, less powerful alkylating agents such as methyl iodide failed to react. Indeed in the current work, all of the aziridines failed to undergo alkylation with methyl iodide even after several days of refluxing.

The alkylated triflate salt, [3.34] isolated by Soobramanien<sup>12</sup> could subsequently undergo a number of useful synthetic transformations. An example is given in Scheme 3.8.



**Scheme 3.8**

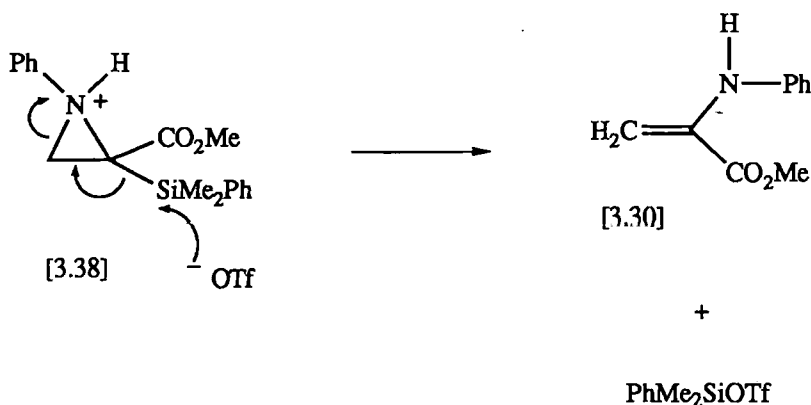
There are a number of possible mechanisms for the reaction of the aziridinium salt with methoxide ion to give a ring opened desilylated product, [3.36]. The absence of a ring opened adduct which had not desilylated indicates that desilylation to give [3.35], rather than ring opening is the preferred initial mode of attack of methoxide ion. This would be followed by an S<sub>N</sub>1 type opening to give a carbonium ion intermediate, [3.37] which is subsequently solvolized to give [3.36].

Alternatively nucleophilic attack of methoxide on the silicon of the aziridinium salt could result in the initial formation of an enamine which subsequently undergoes solvolysis to yield the product.

Most of the aziridines synthesized during the course of this current work were reacted with triflates. The aim was to obtain an overview of the kind of chemistry involved in such systems. A series of reactions was therefore performed, although this was not exhaustive and leaves open an interesting opportunity for further study.

It is expected that the first step in the reaction of an aziridine with triflic acid will be rapid protonation to give an intermediate aziridinium salt. Although the triflate ion is known to be an extremely weak nucleophile, no intermediate aziridinium salt could be detected. The ring opening reaction of 1-carboethoxy-2-trimethylsilylaziridine, [3.4] with triflic acid to give [3.28a], Scheme 3.7, most likely follows a similar mechanism to that for ring opening with halogen acids.

A completely different route is taken when 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine, [3.29] is treated with triflic acid. This reaction leads to the formation of an enamine, [3.30] (Equation 3.2).



Equation 3.2

It is not clear whether this reaction takes place by an  $S_N1$  mechanism (where ring opening precedes attack of triflate) or by an  $S_N2$  route (where triflate attack is simultaneous with or precedes ring opening). Although an  $S_N1$  mechanism would lead to a carbonium ion in the  $\beta$ -position relative to the silicon moiety, its formation is not promoted. This is because hyperconjugative stabilization of a developing positive charge, requires coplanar alignment of the C-Si and  $\beta$ -C-N bonds - an arrangement which is impeded by the constraints of the ring. Also if the  $\beta$ -effect were playing a dominant role, one might possibly expect to observe the formation of a small amount of the triflate adduct. However, complete conversion to the enamine is observed.

In conclusion, enamine [3.30] is most likely formed by an  $S_N2$  mechanism involving an aziridinium salt, [3.38], in which oxygen-silicon bond formation is simultaneous with, or precedes carbon-nitrogen bond breaking (Equation 3.2).

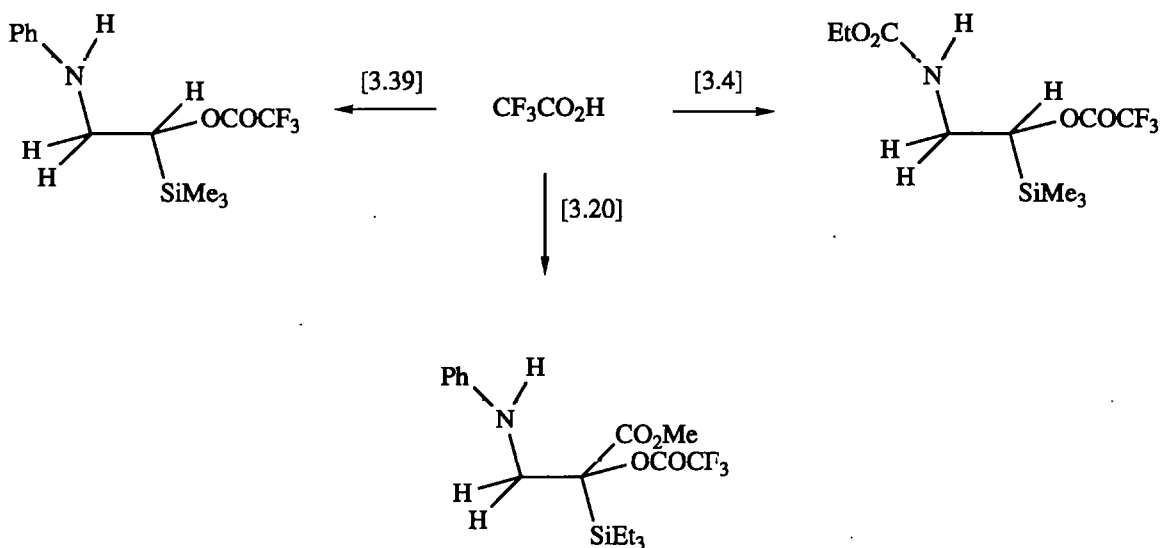
Slightly different results again were obtained when these two silylaziridines were treated with methyl triflate. Whereas the *N*-carboethoxyaziridine, [3.4] gave, cleanly, the ring opened product [3.28a], 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine [3.29] gave a mixture of the ring opened product, [3.32] and a ring opened methylated triflate salt, [3.33], Scheme 3.7.

Only one of the aziridines, 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine, [3.29] was reacted with trimethylsilyl triflate (Scheme 3.7). In this case ring opening did not occur but an aziridinium salt, [3.31] was formed, which was stable for several hours under the conditions of the reaction. Whereas the other reactions of triflates with the aziridines gave the products immediately, trimethylsilyl triflate reacts relatively slowly with the aziridine studied to give the silylated aziridine, with the reaction reaching completion after several minutes.

There is no obvious explanation for the difference in reactivity of the triflates towards the aziridines and of the aziridines towards the triflates.

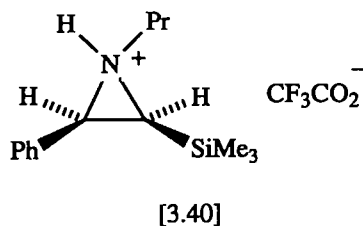
### 3.5 Ring opening reactions with trifluoroacetic acid

In common with triflic acid, trifluoroacetic acid is a strong acid and provides an anion of low nucleophilicity. However the anion is somewhat more basic than the triflate anion and probably more nucleophilic. As might have been predicted, through consideration of the reactions of triflates with the aziridines, only the products of  $\alpha$ -ring opening were observed with aziridines [3.39], [3.4] and [3.20].



Scheme 3.9

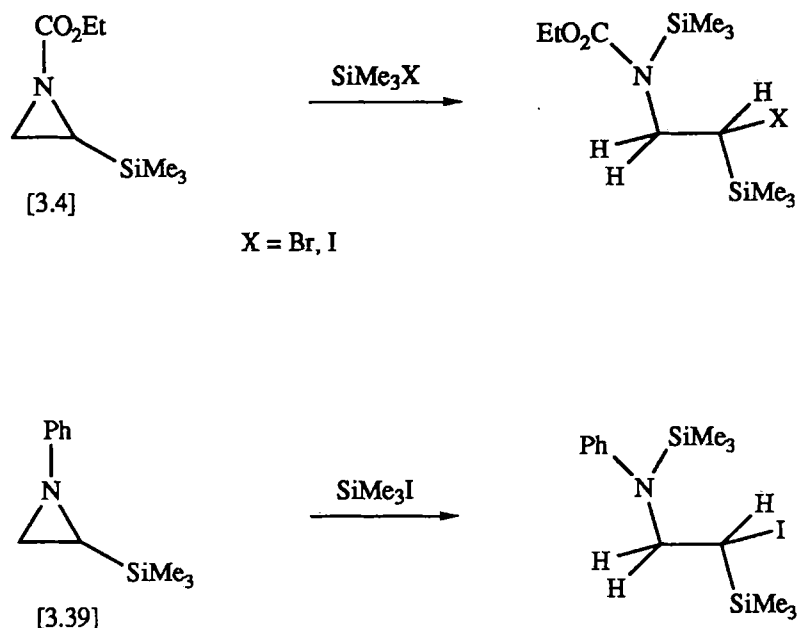
In a previous study<sup>12</sup> of the reaction of trifluoroacetic acid with silylaziridines a stable protonated trifluoroacetate salt, [3.40] was isolated and crystallized.





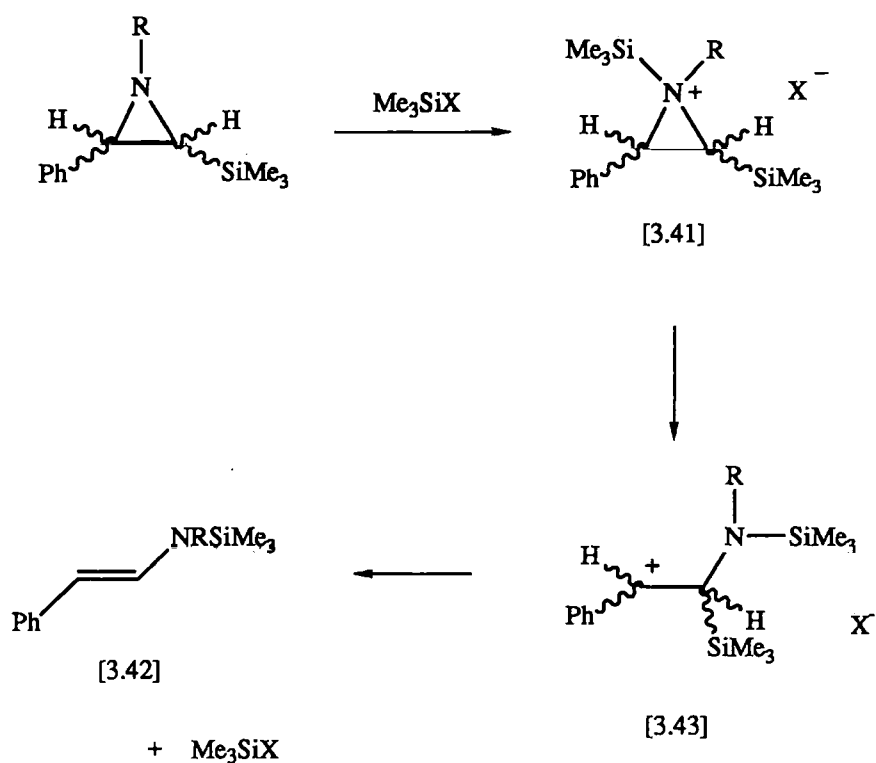
### 3.6 Ring opening of silylaziridines with trimethylsilyl halides

1-Carboethoxy-2-trimethylsilylaziridine, [3.4] and 1-phenyl-2-trimethylsilylaziridine, [3.39] reacted quantitatively with trimethylsilyl bromide or trimethylsilyl iodide to give the corresponding  $\alpha$ -ring opened products (Scheme 3.10).



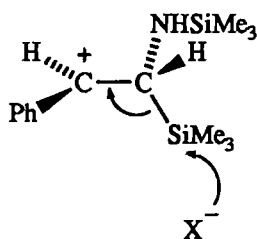
Scheme 3.10

The reactions were carried out at  $-5\text{ }^{\circ}\text{C}$  in deuteriochloroform under nitrogen in sealed NMR tubes. There was no evidence for the presence of an enamine, produced by catalytic attack of the trimethylsilyl halide, as has been observed previously. Soobramanien<sup>12</sup> has studied the reactions of these halosilanes with three aziridines, *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine, and *cis* and *trans*-1,3-diphenyl-2-trimethylsilylaziridines. Each reacted readily with stoichiometric or catalytic amounts of trimethylsilyl bromide or iodide to give *trans* enamines, [3.42]. It had been rationalised that the enamines result from initial attack of the nitrogen lone pair on the silicon atom of the halide, to give a quaternary salt, [3.41]. A carbonium ion, [3.43] is then generated by  $\beta$ -cleavage. Subsequently, attack by iodide ion gives the enamine with release of the trimethylsilyl halide (Scheme 3.11).

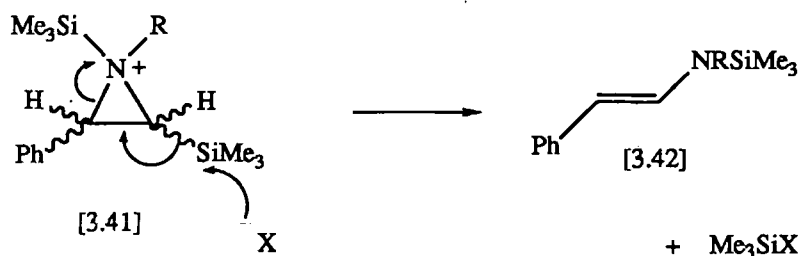


Scheme 3.11

The preferred formation of the *trans* enamines in these reactions may be explained in terms of smaller steric interactions in the carbonium ion intermediate where the phenyl group and nitrogen are as far apart as possible as shown below.

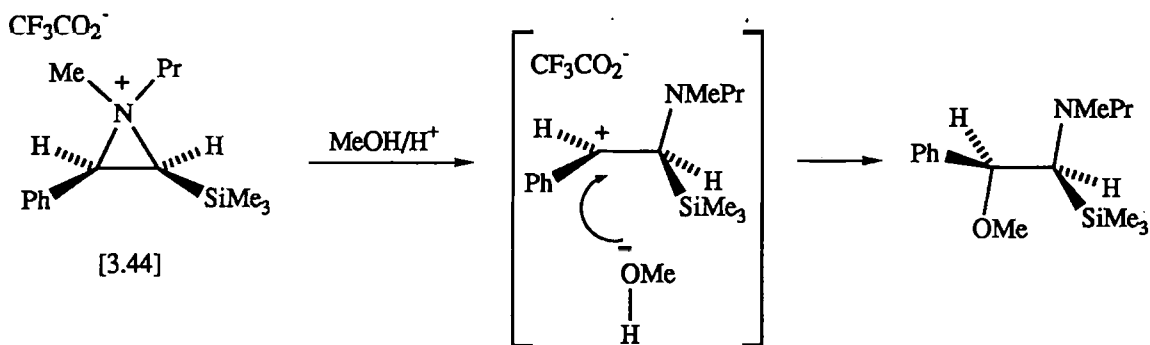


It is also possible that iodide attack is simultaneous with or precedes the ring opening step (Equation 3.3).



Equation 3.3

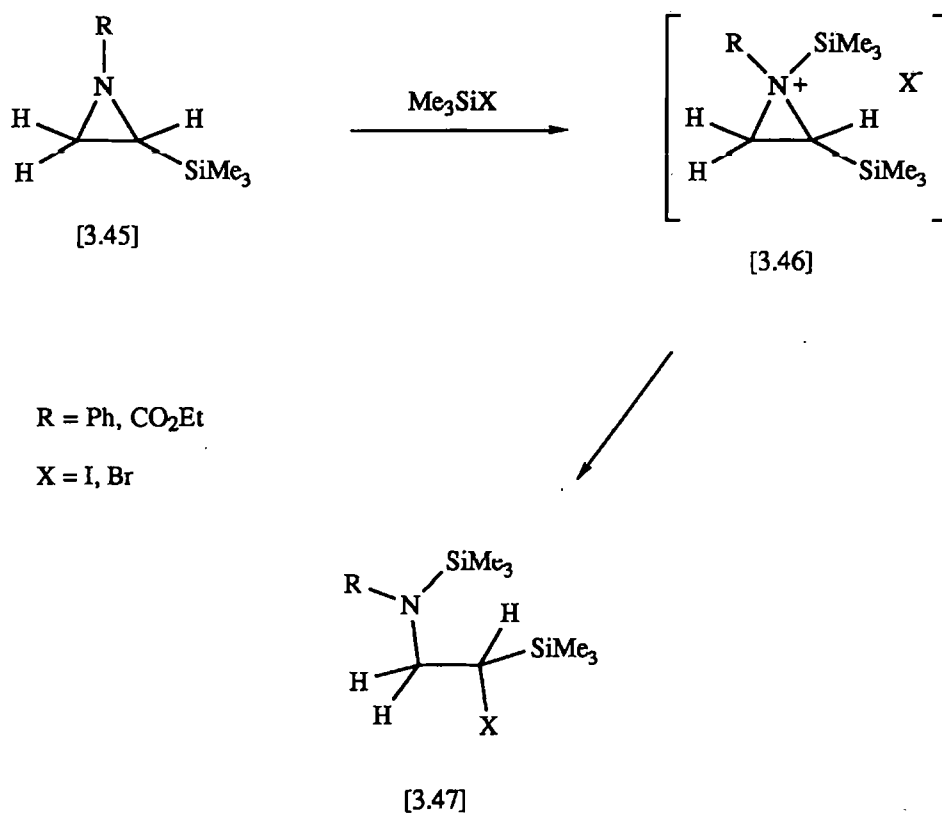
However, the fact that a *trans*-*N*-silylamine was formed from both the *cis* and the *trans* aziridines suggests that the ring opening step occurs prior to attack by iodide; that is, unless isomerization of the *cis* product to yield the more favoured *trans* form occurs. The two aziridines [3.4] and [3.39] studied in the current work showed no evidence whatever of formation of an enamine, giving only products of ring opening. If the S<sub>N</sub>1 route described by Soobramanien is valid, it follows that for our aziridines, the rate of ring opening (S<sub>N</sub>2) by α-cleavage is much greater than the rate of β-cleavage to generate a carbonium ion intermediate. This could be explained in terms of substituent effects with [3.4] and [3.39]. With these aziridines, there is no substituent which is capable of stabilizing either a β-carbonium ion intermediate (which would lead to an enamine), or positive charge build up on the transition state for β-ring cleavage. The result is a preference for α-cleavage by an S<sub>N</sub>2 route. However, with the 3-phenyl substituted aziridines studied by Soobramanien<sup>12</sup>, the incipient carbocations are stabilized by the phenyl group. A similar effect has been observed in a few other cases, an example being the reaction of a methylated trifluoroacetate salt, [3.44] with methanol (Scheme 3.12).



Scheme 3.12

Here positive charge build up on the central carbon atom in the intermediate or transition state is stabilized by the phenyl group (to a greater extent than it is stabilized by the influence of the  $\alpha$ -silyl group). It must be noted though, that these are exceptional cases. In all of the current work and most of the previous work on ring opening of silylaziridines and silylepoxydes,  $\alpha$ -cleavage is consistently observed, the stabilization of negative charge in the transition state being a predominant effect.

In conclusion, the suggested mechanism for the formation of the observed products ([3.47]) obtained from the reactions of aziridines, [3.45] with trimethylsilyl halides, is therefore attack of the nitrogen lone pair on the silicon atom of the trimethylsilyl halide to give an intermediate aziridinium salt, [3.46] which is subsequently ring opened by nucleophilic attack of the halide ion to give [3.47] (Scheme 3.13).

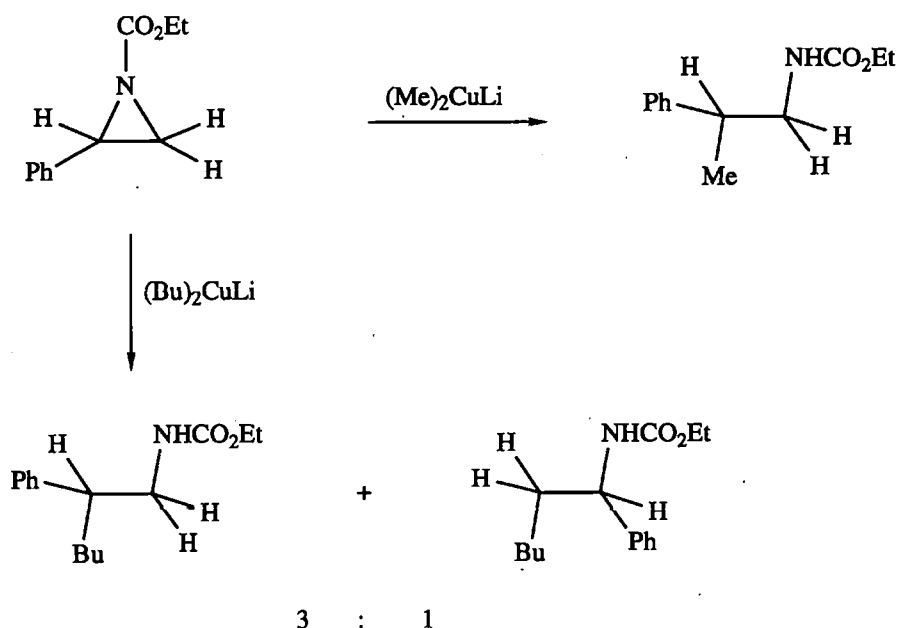


**Scheme 3.13**

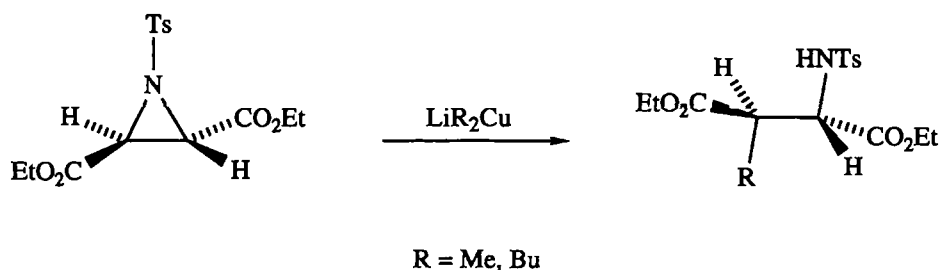
### 3.7 Reactions of silylaziridines with nucleophilic reagents

#### 3.7.1 Introduction

Nucleophilic ring opening reactions of silylaziridines have thus far not been discussed in the literature. However the behaviour of non-silyl substituted aziridines towards nucleophiles has been well covered. While aziridines and epoxides undergo electrophilic ring opening with relative ease, they are fairly stable towards nucleophilic reagents. Nevertheless, such reactions have been accomplished under appropriate conditions. The outcome can depend on the nucleophilicity of the attacking reagent, the degree of 'activation' in the aziridine, and the reaction conditions (usually quite forcing). In view of the work that has been done in the past, it was decided to synthesize silylaziridines that would be most likely to be susceptible to reactions with nucleophilic reagents, and to choose nucleophiles which had been employed successfully in the past. An example where nucleophilic ring opening has been applied successfully in the past, and is well documented, concerns the reaction of epoxides <sup>20-22</sup> and aziridines (Scheme 3.14<sup>23</sup> and Equation 3.4<sup>24</sup>) with organocuprate reagents.



Scheme 3.14



Equation 3.4

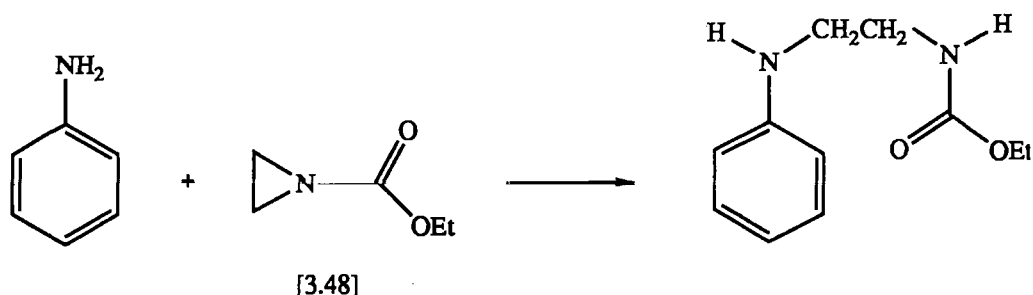
The nucleophilic ring opening reactions of epoxides with organometallic reagents constitutes a useful synthetic method but it is limited in scope due to competing reactions arising from either the Lewis acidity or basicity of the organometallic reagent. Organocuprates in particular, have been found to be far superior when compared with organolithium and Grignard reagents in the nucleophilic ring opening of epoxides<sup>25</sup>. This is in part due to the mild conditions which may be employed. An important consideration in the current work, was the observation that lithium diorganocuprates could selectively ring open epoxides in the presence of unprotected carbonyl functions<sup>26</sup>. This can be explained in terms of hard and soft acid-base theory. Lithium dialkyl cuprates are softer bases than the corresponding alkyl lithiums. So it was expected that aziridines such as 1-carboethoxy-2-trimethylsilylaziridine would lead to ring opened products with lithium dibutyl cuprate, whereas the same aziridines had undergone reaction at the carbonyl site with *n*-butyllithium. It should be noted that the cuprate reactions may involve electrophilic assistance by lithium and so do not represent true nucleophilic displacements and that the nucleophilic site is actually the copper atom.

Other nucleophilic aziridine ring opening reactions that have been employed successfully include those with amines<sup>27</sup>, enolates<sup>28</sup>, and Wittig reagents<sup>29</sup>.

Generally ring opening reactions of aziridines by direct nucleophilic attack have been shown to proceed extensively if not entirely, with inversion of configuration at the point of

attack<sup>1</sup>. Steric influences are an important consideration with a preference for attack at the least substituted carbon atom<sup>3</sup>.

Aziridines of the type [3.48] have been observed to react under relatively mild conditions (3 days at 50 °C, ethanol as solvent), with aniline which is itself relatively weakly nucleophilic (Equation 3.5).

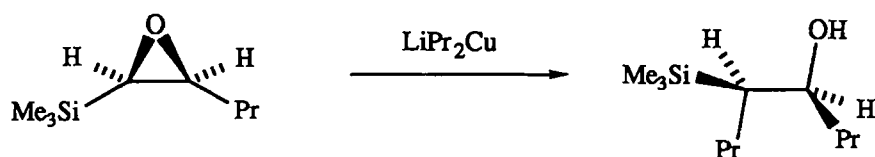


Equation 3.5

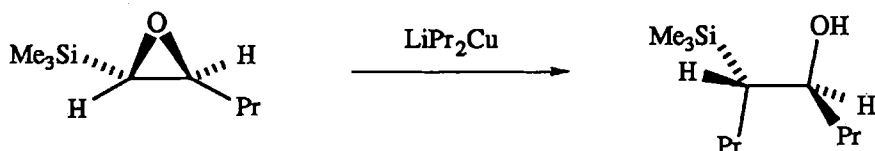
Kinetic data for this experiment are consistent with a mechanism involving bimolecular displacement by the aniline nitrogen on the aziridine carbon. Furthermore, with electron supplying groups on the aniline, an increased rate is observed while electron withdrawing groups cause a decrease in rate.

### 3.7.2 Nucleophilic ring opening reactions of silylepoxides

In common with ordinary epoxides and also aziridines, silylepoxides do not undergo ring opening by direct nucleophilic attack with ease. In many cases, such reactions proceed only with the assistance of electrophilic (e.g., Lewis acid) catalysis. Organocuprates have been applied successfully in the ring opening reactions of silylepoxides and as such have provided the first method for the regio and stereospecific synthesis of  $\beta$ -hydroxyalkylsilanes<sup>29</sup>. Ring opening occurs exclusively by  $\alpha$ -cleavage (Equations 3.6 and 3.7).

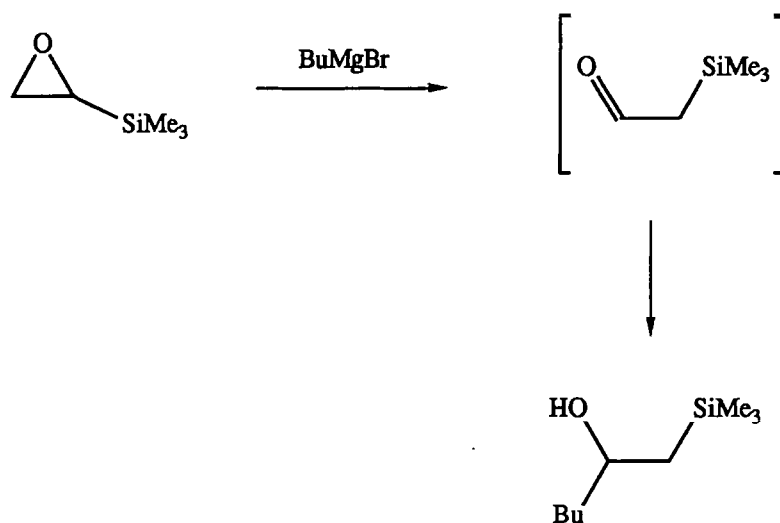


Equation 3.6



Equation 3.7

$\beta$ -Hydroxysilanes have also been produced<sup>30</sup> by the action of Grignard reagents on silylepoxides. However, this involves an initial Lewis acid catalyzed rearrangement of the epoxides to  $\alpha$ -silyl aldehydes or ketones, followed by *in situ* trapping by the Grignard reagent (Scheme 3.15).

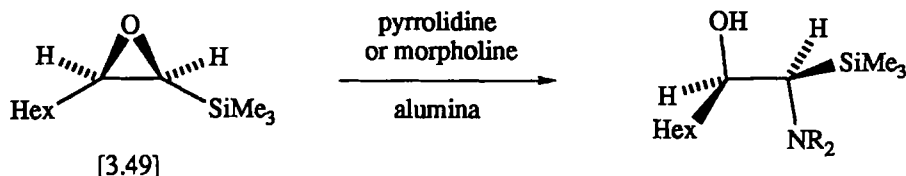


Scheme 3.15

Clean ring opened products have also been obtained by the action of pyrrolidine or morpholine on *cis*-1-trimethylsilyl-1-octene oxide ([3.49], Equation 3.8)<sup>18</sup>, however, the



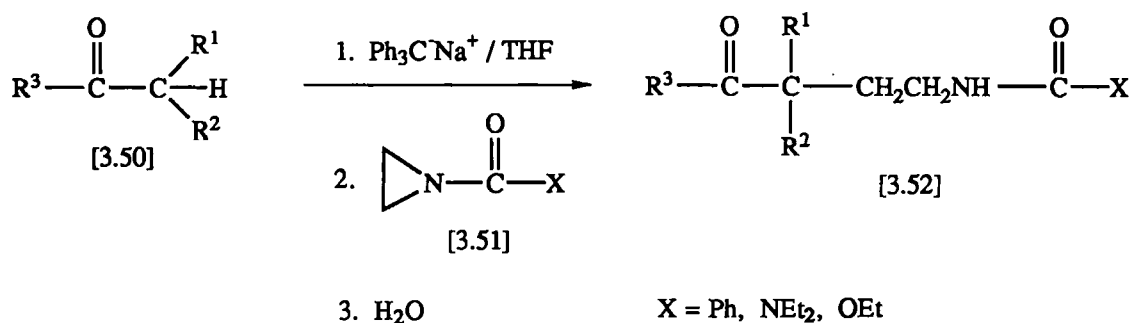
reaction was not feasible in the absence of alumina assistance. (The *trans* epoxide was inert to these conditions).



Equation 3.8

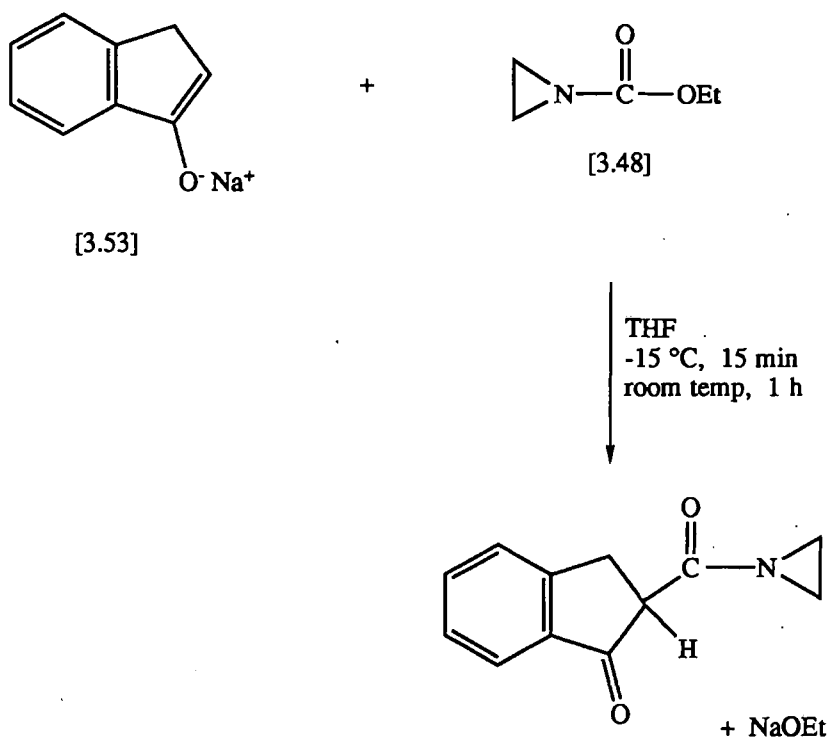
### 3.7.3 Competition between ring opening and reaction at a carbonyl group

Many of the aziridines which are activated towards nucleophilic ring opening, such as the carboalkoxy aziridines which have been studied here, are also susceptible to reaction at the substituent. This situation is particularly problematic when the substituent on nitrogen is a carbonyl group. The distortion from planarity imposed by the ring structure inhibits conjugation of the lone pair on nitrogen with the carbonyl group. The result is that the carbonyl group is more ketone or ester like, than amide or carbamate like, rendering it more electrophilic and susceptible to nucleophilic attack. Also, the carbonyl carbon is hard in character, whereas the ring carbon represents a softer site. The regiochemistry of attack can therefore depend on the nature of the attacking nucleophile. Previous studies have shown that competition does arise between attack at the substituent and attack at the ring carbon in the reactions of such aziridines with nucleophiles. Stamm and Weiss<sup>31</sup> report a series of reactions of ketone enolates derived from [3.50] with *N*-carbonyl aziridines, [3.51] (Scheme 3.16). It was found that ring opening to give [3.52] was the preferred mode of attack, only when the enolate was sufficiently soft in character, e.g., when an  $\alpha$ -aryl substituent was present.



Scheme 3.16

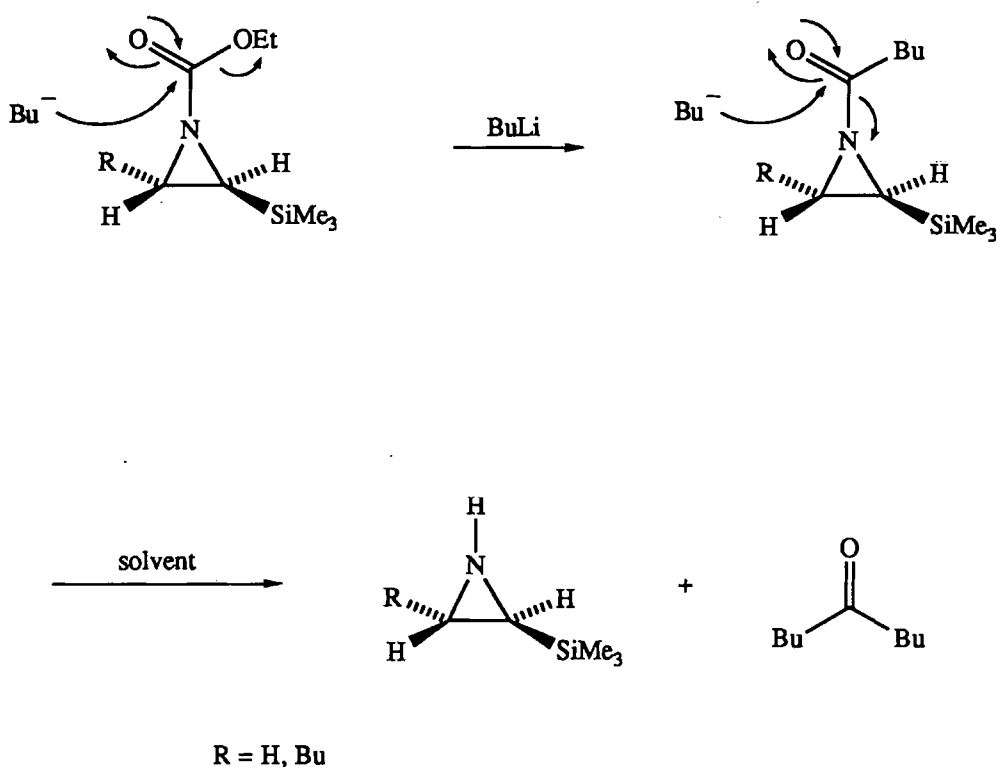
With harder enolates such as that derived from 1-indanone, [3.53], carbonyl attack on [3.48] predominates (Equation 3.9).



Equation 3.9

Hassner and Kascheres<sup>32</sup> have also reported the competitive attack at a ring carbon versus a carbonyl in aziridinecarbamates. In a corollary to the hard-soft acid-base theory explanation just described, they have proposed that nucleophilicity governs the course of

the reaction; better nucleophiles attacking at the carbonyl function and the weaker nucleophiles attacking the ring carbon. Trityllithium, a strong base but weak nucleophile, attacks exclusively at the ring carbon of ethyl aziridinecarbamate, [3.48], whereas lithium amides, such as lithium diisopropylamide or lithium diphenylamide, afford exclusively products arising from carbonyl attack. Indeed, in the current work, addition of *n*-butyllithium to aziridinecarbamates led to the quantitative production of 5-nonanone (Scheme 3.17).



Scheme 3.17

Another interesting finding in the current work was the observation that lithium aluminium hydride reacts exclusively at the carbonyl site. The reactions were carried out in ether with an excess of lithium aluminium hydride. In the case of 1-carboethoxy-2-trimethylsilylaziridine, depending on the conditions used, reduction gave either the *N*-unsubstituted aziridine or the *N*-hydroxymethyl aziridine. Under rigorously dry conditions, complete reduction to the aziridine was observed, whereas when slightly moist

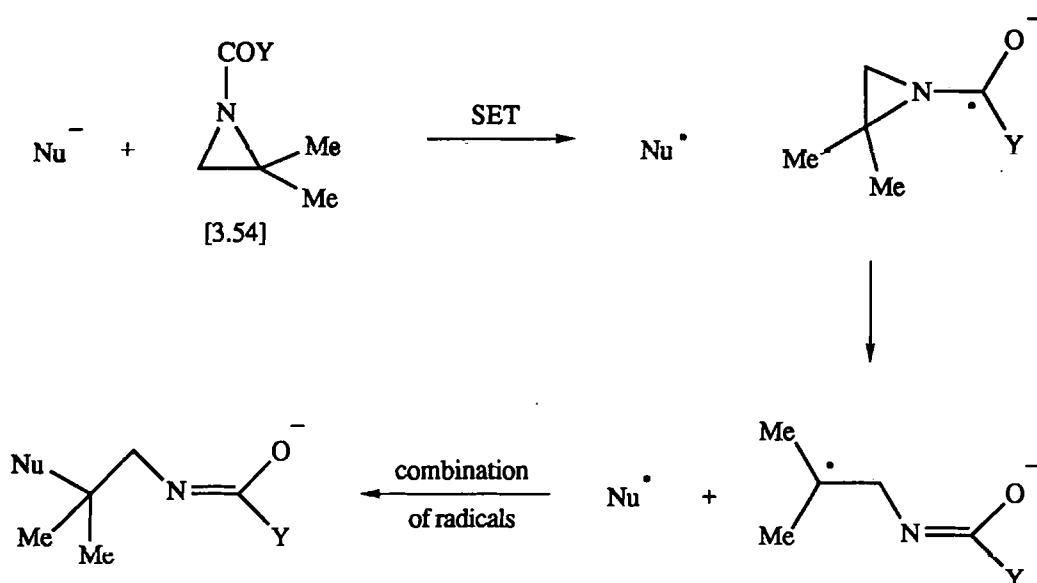
ether was used, only partial reduction took place. It is thought that the hydroxymethyl aziridine is an intermediate in the production of the fully reduced aziridine. The hydroxymethyl compound was obtained in good yield, although it decomposed when distillation was attempted. It is too volatile to purify by chromatography to an analytical standard. Remarkably, this aziridine is stable under aqueous conditions, although it might be expected to eliminate formaldehyde. There was no obvious reason for this outcome.

Normally, reduction of tertiary amides by lithium aluminium hydride leads to the secondary amine<sup>33</sup>. Under controlled conditions however it is possible to obtain the corresponding aldehydes<sup>34</sup>. Similarly, Brown and Tsukamoto<sup>35</sup> have reported that 1-acylaziridines can be reduced to aldehydes with lithium aluminium hydride.

A different result was obtained in the reaction of *trans*-3-butyl-1-carboethoxy-2-trimethylsilylaziridine. Here complete reduction to the *N*-unsubstituted aziridine is observed, even under quite moist conditions. There is no clear explanation for the observed outcome.

#### 3.7.4 SET mechanism in aziridine ring cleavage

Occasionally, a marked change in the high regioselectivity of aziridine ring opening is observed which represents a change from a sterically decelerated S<sub>N</sub>2, to a SET (single electron transfer) mechanism, with homolytic ring opening and radical combination<sup>27,36,37</sup>. This situation has been observed in some 2,2-disubstituted aziridines such as [3.54], where an activating substituent is present on the nitrogen atom as in Scheme 3.18<sup>27</sup>. The abnormal ring openings of these aziridines resembles a nucleophilic substitution in the neopentyl position which itself would be very slow. With poor activating groups on the nitrogen, an S<sub>N</sub>2 reaction will be extremely slow, enabling a SET to occur. Only with good activating groups on the nitrogen is the S<sub>N</sub>2 ring opening, albeit at the CH<sub>2</sub> group, sufficiently faster than the SET.



Scheme 3.18

### 3.7.5 Reaction of silylaziridines with nucleophilic reagents

Whereas the behaviour of silylepoxydes and non-silylaziridines towards nucleophilic reagents is reasonably well covered in the literature, there are no reports of successful, nucleophilic ring opening reactions of silylaziridines. Soobramanien<sup>12</sup> has carried out a number of reactions of silyaziridines with nucleophiles but in all cases the starting material has been recovered almost quantitatively. The reactions attempted include that of *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine with lithium aluminium hydride, sodium methoxide or lithium di-*n*-butylcuprate/boron trifluoride etherate, and *cis*-1,3-diphenyl-2-trimethylsilylaziridine with pyrrolidine in the presence of alumina or boron trifluoride etherate.

The previous failure of any of the silylaziridines to react with nucleophilic reagents prompted us to synthesize silylaziridines which should be activated towards nucleophilic ring opening. The aziridines chosen were ones with an *N*-carboethoxy substituent (an

'activated' aziridine in the terminology of Hamm) and others with an ester substituent in the 2-position. Both of these classes of aziridine have the ability to stabilize negative charge build up on the central carbon atom in the transition state for ring opening. A number of reactions of these aziridines with nucleophilic reagents were attempted, however, no products of ring opening were observed, the starting materials being recovered quantitatively. Some nucleophilic reactions did take place at the carbonyl function in the carboethoxy aziridines (*viz* reactions of lithium aluminium hydride and *n*-butyllithium). Reactions were attempted using a Grignard reagent (methyl magnesium iodide); organocuprate (lithium di-*n*-butyl cuprate); amines (aniline/ethanol, reflux, benzylamine/ethanol, reflux) and diethylmalonate anion. The reactions were carried out under various conditions but none was successful, the starting materials being recovered completely unreacted.

That no nucleophilic ring opening reactions were successful is in itself significant. Aziridines possessing an *N*-carboethoxy substituent have been shown to undergo nucleophilic reactions under mild conditions with relatively weak nucleophiles, yet when a 2-trialkylsilyl group is present the starting aziridines are recovered quantitatively. This unexpected outcome is best explained in terms of the steric influence of the bulky silyl groups, approach of the nucleophile being hindered at the 2-position. Although this will also be the case for electrophilic ring opening of the same aziridines, the energy of the transition state for ring opening here is lowered due to coordination at nitrogen.

By analogy of the work of Baldwin on ring opening of aziridine-2-carboxylates, with organometallic<sup>38</sup> and Wittig<sup>28</sup> reagents it might be expected that if nucleophilic ring opening of the  $\alpha$ -carboethoxy aziridines is not successful at C-2, then attack could still occur at the sterically less hindered C-3 Carbon. The observed failure in this case may be due to the electronic effect of the silicon which may have a destabilizing effect on the transition state for attack at this carbon.

### 3.8 References

1. R. Ghirardelli and H. J. Lucas *J. Am. Chem. Soc.* **79**, 734, (1957).
2. G.E. Ham, *J. Org. Chem.*, **29**, 3052, (1964).
3. R.E. Parker and N.S. Isaacs, *Chem. Rev.*, 737, (1959).
4. J.F. Bunnett, R.L. McDonald, F.P. Olsen, *J. Am. Chem. Soc.*, **96**, 2855, (1974).
5. N.J. Leonard and K. Jann, *J. Org. Chem.*, **28**, 4806, (1962).
6. W. Koch, G. Frenking and H. Schwarz, *J. Chem. Soc., Chem. Commun.*, 1119, (1985).
7. A.C. Hopkinson and M.H. Lien, *J. Org. Chem.*, **46**, 998, (1981).
8. O.C. Dermer and G.E. Ham, "Ethyleneimine and other Aziridines", Academic Press Inc., New York, 1969, p. 263-267.
9. Y. Iwakura and A. Nabeya, *J. Org. Chem.*, **25**, 1118, (1960).
10. C. Eaborn, F. Feichtmayr, M. Horn, and R.J. Murrell, *J. Organomet. Chem.*, **77**, 39, (1974).
11. A.R. Bassindale and P.G. Taylor in "The Chemistry of Organic Silicon Compounds, Part 2", Ed. S. Patai, p. 904-905.
12. M.C.C. Soobramanien, Ph.D Thesis, The Open University, Milton Keynes, (1988).
13. J. J. Eisch and J. T. Trainor, *J. Org. Chem.*, **28**, 2870, (1963).
14. P.F. Hudrlik, D. Peterson, R.J. Rona, *J. Org. Chem.* **40**, 1755, (1975).
15. P.F. Hudrlik, A.M. Hudrlik, R.J. Rona, R. N. Misra and G.P. Withers, *J. Am. Chem. Soc.*, **99**, 1993, (1977).
16. A. P. Davis, G.J. Hughes, P.R. Lowndes, C.M. Robbins, E.J. Thomas and G.H. Whitham, *J. Chem. Soc., Perkin Trans. 1*, 1934, (1981).

17. G. Berti, S. Canedole, P. Crotti and F. Macchia, *J. Chem. Soc., Perkin Trans. I*, 1183, (1984).
18. P.F. Hudrlik, A.M. Hudrlik, and A.K. Kulkarni, *Tetrahedron Lett.*, 139, (1985).
19. P.J. Stang and M.R. White, *Aldrichimica Acta*, 16, 14, (1983).
20. B.C. Hartman, T. Livinghouse, and B. Rickborn, *J. Org. Chem.*, 38, 4346, (1973).
21. B.H. Lipshutz, R.S. Wilhelm, J. Kozlowski, and D. Parker, *J. Org. Chem.*, 49, 3928, (1984).
22. R.W. Herr, D.M. Wieland, and C.R. Johnson, *J. Am. Chem. Soc.*, 92, 3813, (1970).
23. A.P. Kozikowski, H. Ishida and K. Isobe, *J. Org. Chem.*, 44, 2788, (1979).
24. D. Tanner, C. Birgersson, and H.K. Dhaliwal, *Tetrahedron Lett.*, 1903, (1990).
25. E. Erdick, *Tetrahedron*, 40, 641, (1984).
26. C.R. Johnson, R.W. Herr, and D.M. Wieland *J. Org. Chem.*, 38, 4263, (1973).
27. H. Stamm, P. Assithianakis, B. Bucholz and R. Wieß, *Tetrahedron Lett.*, 23, 5021, (1982).
28. J.E. Baldwin, R.M. Adlington and N.G. Robinson, *J. Chem. Soc., Chem. Commun.*, 153, (1987).
29. P.F. Hudrlik, D. Peterson and R.J. Rona, *J. Org. Chem.*, 40, 2263, (1975).
30. P.F. Hudrlik, A.M. Hudrlik, R.N. Misra, D. Peterson, G.P. Withers and A.K. Kulkarni, *J. Org. Chem.*, 45, 4444, (1980).
31. H. Stamm and R. Weiss, *Synthesis*, 392, (1986).
32. A. Hassner and A. Kascheres, *Tetrahedron Lett.*, 4023, (1970).
33. R.F. Nystrom, and W.G. Brown, *J. Am. Chem. Soc.*, 70, 3738 (1948).



34. E. Mosettig, "Organic Reactions", vol 8, Robert E. Krieger Publishing Company, Huntington, New York, 1975.
35. H.C. Brown and A. Tsukamoto, *J. Am. Chem. Soc.*, **83**, 4549, (1961).
36. H. Stamm, P. Assithianakis, *Chem. Ber.*, **120**, 885, (1987).
37. K. Bellos, H. Stamm, D. Speth, *J. Org. Chem.*, **56**, 6846, (1991).
38. J.E. Baldwin, R.M. Adlington, I.A. O'Neil, C. Schofield, A.C. Spivey, and J.B. Sweeney, *J. Chem. Soc., Chem. Commun.*, 1852, (1989).

## CHAPTER 4

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# FLUORODESILYLATION OF SILYLAZIRIDINES

### 4.1 Introduction

One of the principal aims of this study of silylaziridines was to find an effective method of removing the silyl group and to subsequently trap the resultant aziridinyll anions with electrophiles. If successful, such a manipulation would be of major synthetic significance since the reaction is expected to occur with retention of configuration as has been shown to be the case with some silylepoxydes<sup>1</sup>. The original relative configuration of the ring would be retained, and at the same time, new functionality would be introduced. A situation like this is desirable, as it would provide a route to stereochemically pure and highly functionalized aziridines which could then be ring opened to give products of predetermined stereochemistry.

### 4.2 Fluoride ion induced desilylation

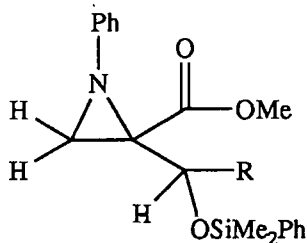
The nucleophilic affinity of fluoride ion for silicon has been well recognised and widely applied in the cleavage of carbon-silicon bonds. This observation can be understood when we consider the strength of the fluorine-silicon bond which is 142 kcal/mol<sup>2</sup>.

Ionic fluorides are in general extremely hygroscopic, and their use as silicon nucleophiles is often dependant on obtaining rigorously anhydrous conditions. The effectiveness of a fluoride source as a desilylating agent depends on a number of factors including water content and solubility. However there remains much confusion in the literature as to the optimum conditions for reaction. Much work has been reported in this area in the last twenty years, but a clear pattern of conditions which promote reaction has not emerged.

Various conditions using a range of temperatures, solvents, reaction times, and quantity of reagents have been used, and it would appear that often, when desilylation (and trapping of the anion) does not occur with ease, these systems have an almost particular set of required conditions. Indeed, in this current work, a vast amount of experimentation was required to find an effective system for the promotion of both the desilylation reaction and the subsequent trapping of the so-formed anion with electrophiles.

The concept of fluorodesilylation is one that is central to this thesis. A detailed account of the work undertaken has therefore been included, and should offer some valuable direction to future workers in a clearly problematic field. A summary here of the strategies involved, and the results obtained will therefore aid understanding of the study.

Although fluorodesilylation of silylaziridines represented a major synthetic goal, it was not anticipated that this objective would meet with such difficulties as were encountered. The aim was not necessarily to produce synthetically useful products, but to develop a method that could be applied in the preparation of highly functionalized compounds. An illustration of this high degree of functionality which could be achieved, can be seen from some of the products, e.g., [4.1a] and [4.1b] that were eventually obtained in the study, where the carbon in the 2-position is considerably functionalized.

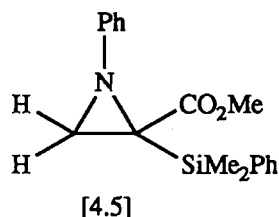
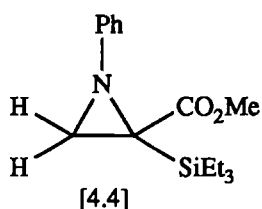
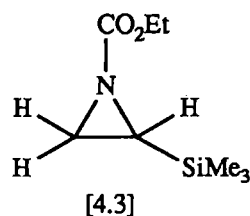
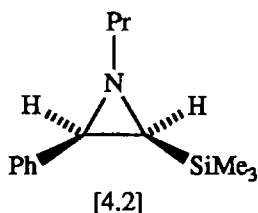


[4.1a],  $R = (CH_2)_4CH_3$

[4.1b],  $R = Ph$

Four aziridines were investigated in this study, *cis*-3-phenyl-1-propyl-2-trimethylsilyl-aziridine, [4.2], 1-carboethoxy-2-trimethylsilylaziridine, [4.3], 2-carbomethoxy-1-phenyl-

2-triethylsilylaziridine, [4.4] and 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine, [4.5].



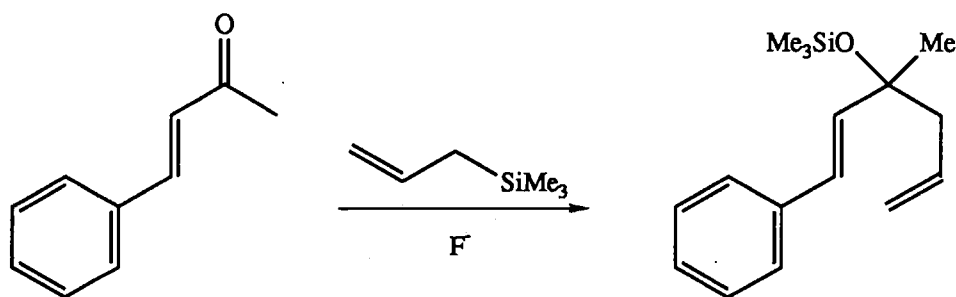
The initial work was carried out on *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine, [4.2]. The failure of this aziridine to desilylate effectively prompted us to look for a more activated aziridine in the form of 1-carboethoxy-2-trimethylsilylaziridine, [4.3]. Much work was done on this compound and the initial poor results were blamed on the inability to develop a truly anhydrous system, in which the fluoride ion would be more nucleophilic and there would be no ready proton source to quench the anion. However, no desilylation could be achieved during the course of that study. Work then moved on to using more activated aziridines [4.4] and [4.5] which were eventually found to be active in desilylation reactions. A method was then developed for promoting successful electrophilic capture. A number of important deductions about the nature of these systems could be made, and these will serve as an aid to future workers.

### 4.3 Sources of fluoride ion and problems with their use

#### 4.3.1 Introduction

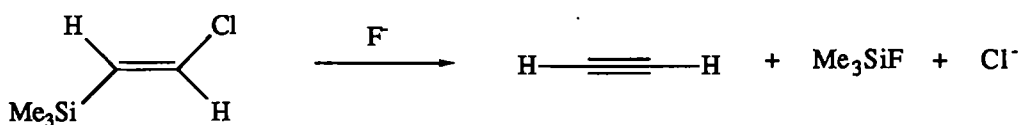
Ionic fluorides<sup>3</sup> are available commercially in a number of different forms, both organic and inorganic. There are a number of problems associated with their use, such as, ease of drying, solubility, and thermal stability, and the suitability of a reagent often depends on the required application. The inorganic fluorides are fairly stable thermally and are usually employed where higher temperatures are required. Organic fluorides such as tetraalkylammonium fluorides tend to be less stable thermally<sup>4</sup> and their use is limited to lower temperatures. Solubility is mostly a problem with inorganic fluorides although there are methods for improving their solubility, even in non-polar solvents, and these will be discussed later.

Considerable spectroscopic<sup>5</sup> and nonspectroscopic<sup>6</sup> evidence suggests that fluoride ion is capable of forming strong hydrogen-bonds to a variety of protic compounds.



Equation 4.1

Fluoride ion therefore finds use as a highly versatile and mild reagent in typically base-assisted reactions, (Equation 4.1)<sup>7</sup>, Michael additions<sup>7,8</sup>, elimination reactions<sup>9,10</sup>, (Equation 4.2)<sup>10</sup>, and condensation reactions<sup>11</sup>.



Equation 4.2

Unfortunately, a consequence of the high base strength of ionic fluorides is that they are extremely hygroscopic, and any water present can severely limit their effectiveness as a nucleophile.

Once dried, the severely hygroscopic nature of ionic fluorides necessitates rapid manipulation in a rigorously anhydrous atmosphere. Any solvents or reagents used in reactions with fluorides must be anhydrous, otherwise the water present will associate with the fluoride, markedly reducing its nucleophilicity. It seems that early work in this thesis may have been unsuccessful owing to sources of moisture in the reaction mixture, even after the need for rigorously anhydrous conditions had been elucidated. The difficulty of obtaining very dry fluoride ion sources was greater than was initially believed. Further work is therefore required in order to be quite certain of the cause of the failure of some of the early work such as that carried out on *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine, [4.2] and 1-carboethoxy-2-trimethylsilylaziridine, [4.3]. It was not within the scope of this thesis to undertake such an exhaustive study. However, considering the work that has been done, the most likely explanation is that the aziridines themselves were deactivated towards desilylation.

#### 4.3.2 Anhydrous sources of fluoride ion

Much of the experimentation eventually centred upon finding a stringently anhydrous method for preparing the fluoride ion. It should be stated that the need for exclusion of moisture in this work appeared to be two-fold. The reasons will be discussed in more detail later, but they are worthy of a brief mention here. Successful desilylation depends on both the reactivity of the silylaziridine towards desilylation, and on the nucleophilicity of

the fluoride ion obtained from different sources. The reactivity of the aziridine will depend on factors such as steric properties, and leaving group ability. The highly activated aziridines could be desilylated under non-anhydrous conditions. It may be the case that the less activated aziridines could be fluorodesilylated successfully if the conditions were completely anhydrous since the fluoride source would be more nucleophilic. The second reason which emerged for the importance of excluding moisture relates to the ability to trap the aziridinyll anion with electrophiles (if indeed the mechanism involves an intermediate aziridinyll anion). The aziridinyll anions have been shown to be highly basic and can preferentially extract a proton from any water (or other proton source) present, rather than react with an electrophile.

A thorough investigation was undertaken in order to find the best anhydrous method and this is described below. All of the solvents were dried, redistilled, stored over 4Å molecular sieves under nitrogen in teflon sealed vials, and used within a few days. The aziridines themselves were dried under high vacuum for several days prior to use. Any electrophiles employed were dried, redistilled and stored under nitrogen, again in teflon sealed vials. It was found that the use of ordinary glassware, round bottomed flasks, *subaseals*, etc., was ineffective in maintaining a rigorously anhydrous atmosphere. The best results were obtained when small vials having teflon seals were used as reaction vessels as well as for storing the reagents. These were dried by heating prior to use and the reagents were introduced by syringe.

#### 4.3.3 Availability of sources of fluoride ion

Alkali metal fluorides, principally potassium fluoride, rubidium fluoride, and cesium fluoride are widely available but they are somewhat expensive. Although relatively easy to dry (heating the salt in a vacuum oven to over 200 °C for several hours is usually sufficient to remove most of the water), their use is rather limited since they are fairly insoluble in most solvents. More recently a more soluble source of ionic fluoride has become available in the form of quaternary ammonium fluoride salts. The most important of these are

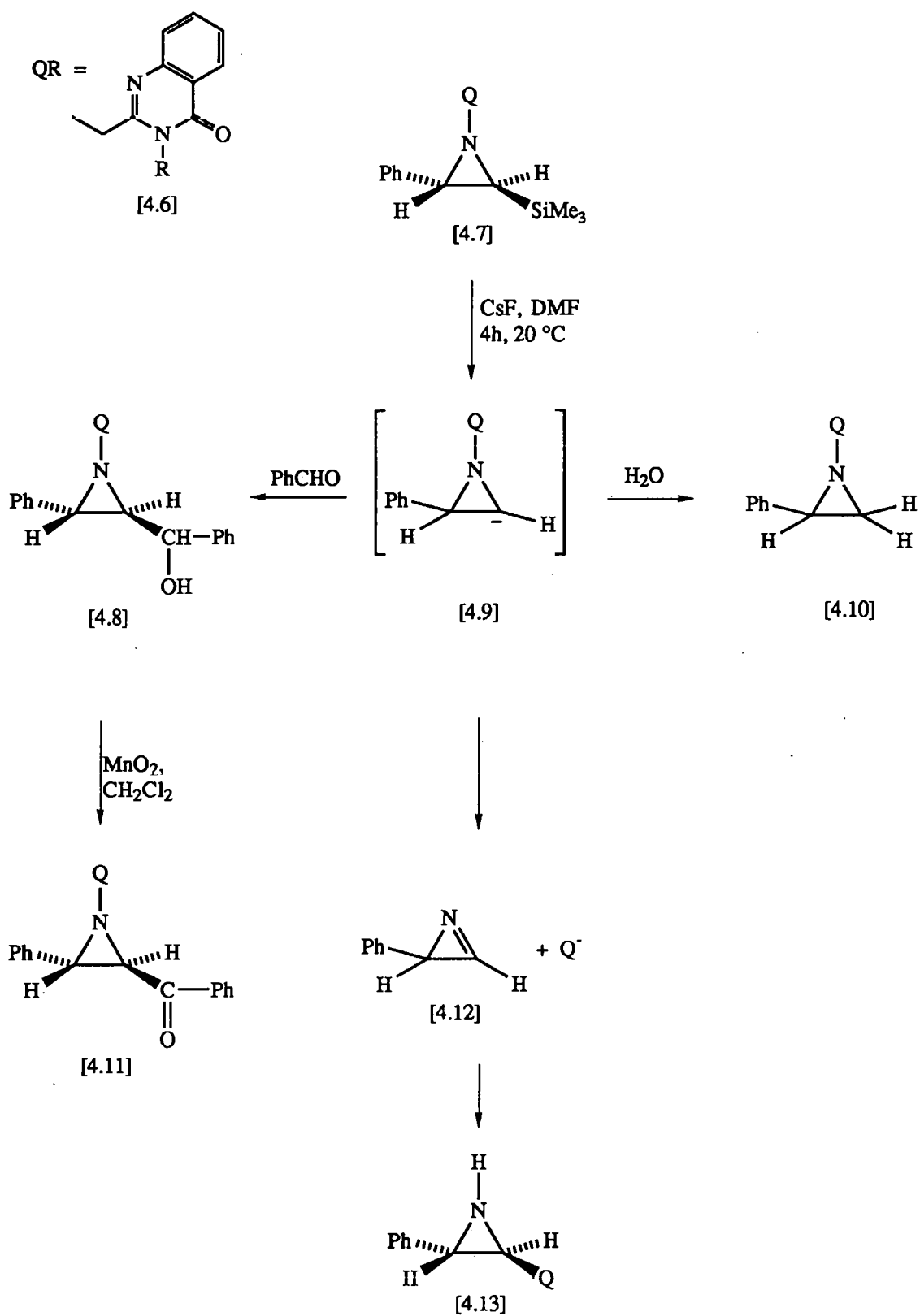
tetrabutylammonium fluoride and tetrabenzylammonium fluoride. However, these compounds are extremely hygroscopic and are difficult, if not impossible to obtain in a completely anhydrous form. Various methods are available for removing water from these salts and their effectiveness will be discussed later. It has been claimed that one fluoride source tris(diethylamino)sulphonium difluorotrimethylsilicate (TASF)<sup>12</sup> can be produced in an anhydrous<sup>13</sup> form but little work with this compound was performed in this study.

#### 4.4 Fluorodesilylation of silylaziridines

Although fluordesilylation reactions in general are well covered in the literature, those of silylaziridines have received little attention and only two incidences have been reported<sup>14,15</sup>. Atkinson<sup>14</sup> has successfully desilylated a silylaziridine. Furthermore, he is the first to report the successful trapping of a desilylated intermediate with an electrophile in such a reaction (Scheme 4.1).

The silylaziridine [4.7]<sup>16</sup> used in this work was one having a quinazolone, [4.6], substituent on the nitrogen. The fluordesilylating agent for the reaction was cesium fluoride with dimethylformamide as the solvent. Under these conditions two products were obtained, a desilylated aziridine, [4.10], thought to be derived through electrophilic capture by water, and a desilylated aziridine, [4.13], thought to be derived from an intermediate azirine, [4.12] which was attacked by the quinazolone anion. In order to test the possibility that aziridine [4.10] had arisen from an electrophilic capture step involving an intermediate aziridinyll anion, the reaction was repeated in the presence of benzaldehyde (3 mol equiv.). In this case, with subsequent oxidation of [4.8], the ketonic aziridine [4.11] was isolated in support of the above suggestion.

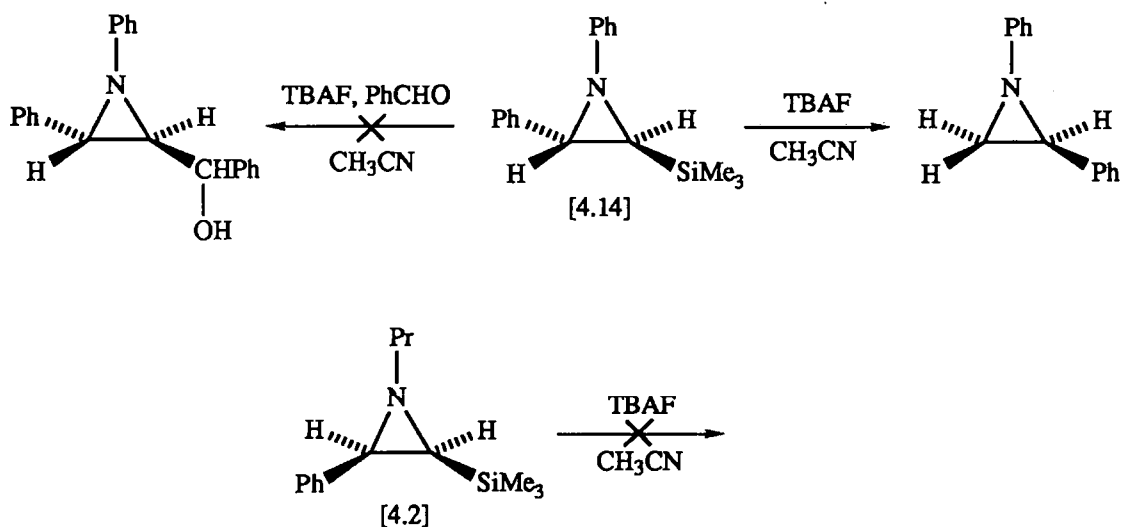




**Scheme 4.1**

Atkinson concluded from these observations that the aziridinyll carbanion, [4.9] is an intermediate in the reaction and that its lifetime is long enough to be captured by a suitable electrophile. However, in the absence of an electrophile an azirine intermediate is formed by elimination of the quinazolone anion. The desilylation reactions reported here seem to occur with relative ease, and do not require an anhydrous system. This is probably due an activating effect from the quinazolone substituent.

Soobramanien<sup>15</sup> has also successfully fluorodesilylated one compound, *trans*-1,3-diphenyl-2-trimethylsilylaziridine, [4.14] using tetrabutylammonium fluoride in acetonitrile under reflux. *Cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine, [4.2] on the other hand failed to desilylate under these conditions. These observations were rationalised in terms of the ability of the substituent on nitrogen to stabilize the intermediate carbanion, with the phenyl group offering a greater stabilizing influence than the propyl group. Clearly further investigation is required, however, an attempt to trap the intermediate carbanion using benzaldehyde as the quenching reagent was unsuccessful (Scheme 4.2).



Scheme 4.2

In this current study, the work of Soobramanien has been extended in order to find a suitable method of desilylating aziridine [4.2], *cis*-3-phenyl-1-propyl-2-

trimethylsilylaziridine, with subsequent electrophilic capture. Simple desilylation procedures such as those described in the literature (including use of alkali metal fluorides in a polar solvent, and tetrabutylammonium fluoride trihydrate in THF) were unsuccessful and the search was begun for an anhydrous source of fluoride ion which might be nucleophilic enough to perform the reaction. It was thought at one stage that an effective method had been obtained using tetrabutylammonium fluoride dried by the method of Cox<sup>17</sup>, but conclusive evidence was not obtained, owing to difficulties in purification and interpretation of the proton NMR data which was complicated by signals from the alkyl groups of the tetrabutylammonium fluoride. It was decided at this stage that the best course of action would be to find an aziridine which would be more activated towards desilylation. The aziridine first used by Soobramanien, and subsequently used in the current work is not activated towards desilylation, probably because the aziridinyl anion represents a very poor leaving group. Thus, it is not surprising that the reactions did not meet with much success.

Another example in the literature which highlights the importance of the leaving group in fluorodesilylation reactions is the difficulty with which the trimethylsilyl-vinyl carbon bond is cleaved<sup>18</sup>. On the other hand cleavage of the silicon-alkynyl bond by fluoride ion, which leads to a less basic anion, is relatively facile. Also, Atkinson's aziridine, [4.7] having an electron withdrawing, *N*-quinazolone substituent had been desilylated with relative ease<sup>14</sup>. It therefore seemed likely that an aziridine which would generate a less basic anion might be more activated towards desilylation. It was thought that replacing the propyl group on nitrogen, which is essentially an electron releasing substituent, with a more electron withdrawing group would make the reaction more favourable (as indeed seemed to be the case with *trans*-1,3-diphenyl-2-trimethylsilylaziridine, [4.14]). Such a situation is attained by placing an ester substituent on the nitrogen atom. 1-Carboethoxy-2-trimethylsilylaziridine therefore seemed to be a hopeful candidate for the reaction. Previous work on desilylation of silylepoxydes<sup>1</sup> has shown that retention of configuration occurs. The intermediate anion therefore has a finite lifetime. The most important stabilizing effect

is probably the inductive withdrawal by the ester substituent which makes the nitrogen atom more electron withdrawing. The nitrogen atom in this aziridine is less basic than a conventional amine since it is essentially part of a carbamate function. The overall effect is to stabilize a negative charge on an adjacent carbon atom.

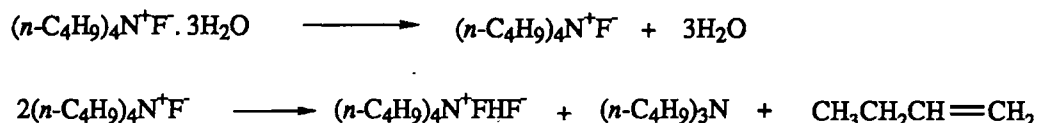
A series of reactions were therefore conducted in the hope of desilylating this aziridine and possibly trapping the anion with electrophiles. At first it was assumed that the reaction would occur with relative ease and so some simple experiments were carried out using potassium or cesium salts as the fluoride source. The alkali metal fluorides have long been known<sup>19</sup> to be strong bases, although their use in synthesis was little realised until the late 1940's. Their activity decreases in the series,  $\text{CsF} \geq \text{RbF} > \text{KF} \gg \text{NaF} > \text{LiF}$ <sup>20</sup>. As a rule of thumb one would expect the desilylation ability to parallel base strength.

No desilylation whatever was observed, the starting aziridine being quantitatively recovered unreacted. The failure of the reaction at this stage could have been due to a number of reasons. Possibly the aziridine was purely unreactive in such reactions. However, it could also be the case that the poor solubility of the fluoride was preventing the reaction. Metal fluorides are sparingly soluble in organic solvents (e.g., solubility of KF in DMSO at 25 °C is 8 mg of fluoride/ 100 g solvent)<sup>10</sup> and often a large quantity of salts and elevated temperatures are required in order to obtain reasonable rates. Often though, fluorodesilylation reactions proceed effectively in the presence of a catalytic amount of fluoride ion so only a small amount is required to dissolve. Also, reactions involving potassium or cesium fluoride may be considered to involve a significant amount of reaction at the surface of the undissolved fluoride<sup>5</sup> and reactions should always be well stirred. However rapid stirring or even treatment with ultrasound proved to be unfruitful. There is evidence though, that reactions involving metal fluoride salts as a source of fluoride ion can be accelerated by the use of crown ethers. Liotta and Harris<sup>21</sup> reported that solubility problems which hamper studies of fluoride ion in weakly solvating media can be overcome by the use of 18-crown-6. This has the effect of rendering the fluoride ion in KF a potent nucleophile both in polar and in non-polar organic solvents. Normally,

reactions involving KF necessitate the use of highly polar solvents, otherwise appreciable ion-pairing severely retards the reaction. In addition, Gingras and Harpp<sup>22</sup> reported that the presence of a catalytic amount of 18-crown-6, or dibenzo-24-crown-8 increases the rate of fluorodestannylation of trialkyltin mercaptides. The use of a crown ether (18-crown-6) in the current work however, failed to promote significantly any reactions involving metal fluorides. Another agent which is known to enhance the activity of potassium fluoride is tetraphenylphosphonium bromide. This reagent accelerates nucleophilic fluorine transfer reactions of potassium fluoride by means of phase transfer catalysis<sup>23</sup>. Good results have been obtained in less polar aprotic solvents such as acetonitrile, but no success was observed when it was employed in the current work with *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine, [4.2].

Solubility problems may not however, be the only reason for the ineffectiveness of metal fluoride salts as desilylating agents in the current work. The nucleophilicity of an ionic fluoride is dependent not only on the solvent in which it is dissolved but also on the amount of water that is present and on the counter ion. Generally tetraalkylammonium fluorides are considered to be superior to the alkali metal fluorides in most nucleophilic reactions, including desilylation reactions. This is due to their good solubility in most organic solvents conferred by the butyl groups in the counterion. The most soluble and indeed the most effective and widely used compound in this class is tetrabutylammonium fluoride. All of these compounds are, however, extremely hygroscopic. This, and their low thermal stability are two of the greatest drawbacks in using tetraalkylammonium fluorides. Commercial tetrabutylammonium fluoride is available as the trihydrate in solid form or in THF. Further drying of this compound is extremely difficult and there is some doubt as to whether it has ever been obtained in a completely anhydrous form. Sharma and Fry<sup>4</sup> have proposed that hydrated tetrabutylammonium fluoride can be dehydrated, but that when the last of the water molecules which stabilize the fluoride are removed, the fluoride, acting as a strong base, initiates a rapid E2 elimination resulting in the formation of the

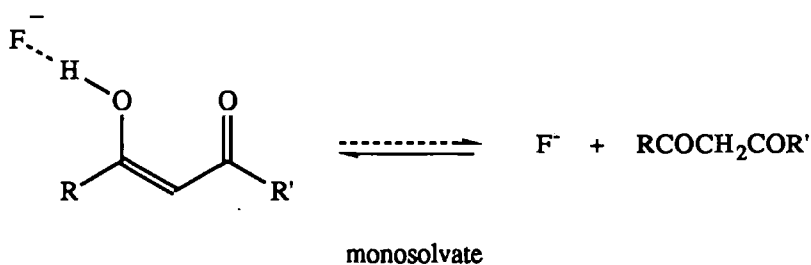
thermodynamically very stable<sup>24,25</sup> bifluoride ion (Equation 4.3). The results which were obtained are based on <sup>19</sup>F and <sup>1</sup>H NMR, and IR spectroscopic data.



Equation 4.3

Despite this problem, a number of methods have been developed which can provide sources of tetrabutylammonium fluoride in a state approaching anhydrous form. A method first described by Cox and co-workers<sup>17</sup>, is generally accepted as being the best for producing 'anhydrous' tetrabutylammonium fluoride. It involves heating the commercially available trihydrate form in a round bottomed flask with stirring under high vacuum (<0.1 mm Hg) at 40-45 °C for 48 hours. The resultant oil, which must be used immediately is said to contain 0.1-0.3 molar equiv of water and *ca.* 10% of tetrabutylammonium bifluoride. When this procedure was repeated in the current work, the final mixture was estimated by weight measurements to contain 1 molar equiv of water. This method proved to be more efficient than prolonged evacuation in a drying pistol which was only successful in removing one equivalent of water at most. Although the sample dried by the method of Cox was a successful desilylating agent in some cases (i.e., with the two α-carbomethoxy aziridines), it could not be employed in cases where an anhydrous source of fluoride was necessary i.e., where addition of electrophiles was required.

Aside from physically removing the water present in an ionic fluoride source, the best method for rendering these compounds anhydrous relies on providing an alternative hydrogen-bond electron acceptor during the evaporation of the aqueous fluoride. In the presence of certain highly acidic compound such as enolizable β-diketones, aqueous solutions of tetraalkylammonium fluorides may be rendered anhydrous by providing a stable non-hygroscopic monosolvate<sup>11</sup>. Such a system is indicated in Equation 4.4<sup>26</sup>.



Equation 4.4

The monosolvate still contains an acidic proton which could quench the aziridiny anion. Perhaps a more convenient method which applies the same principle, involves supporting the fluoride salt on silica gel. The surface of silica gel has many hydroxyl groups and has been shown to be capable of extensive strong hydrogen-bonding to hydrogen-bond electron acceptors and donors<sup>27</sup>. Clark<sup>28</sup> was the first to report that silica-supported tetrabutylammonium fluoride represented a non-hygroscopic source of fluoride and the preparation is now available commercially. It was used without success in the current work in an attempt to desilylate 1-carboethoxy-2-trimethylsilylaziridine. It was possible to fluorodesilylate the more activated ( $\alpha$ -carbomethoxy) aziridines using this reagent but, it was not possible to trap the resultant anions with electrophiles.

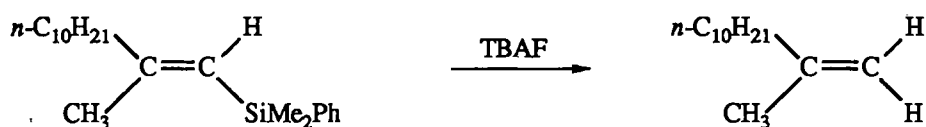
Another method for rendering tetrabutylammonium fluoride anhydrous used in this current work, involves drying a commercial 1.0M solution of tetrabutylammonium fluoride in THF with 4Å molecular sieves. Kuwajima<sup>29</sup> has effectively used 4Å molecular sieves to 'dry' a THF solution of benzyltrimethylammonium fluoride (as shown by yield enhancement in the reaction of enol silyl ethers with alkyl halides). Gingras<sup>30</sup> has used 3Å molecular sieves to dry tetraethylammonium fluoride solutions. Majetich<sup>7</sup> has used 4Å molecular sieves in order to dry DMF solutions of tetrabutylammonium fluoride. This method, of drying with 4Å molecular sieves was actually found to be the most effective way of drying tetrabutylammonium fluoride and led to the most anhydrous and nucleophilic source of fluoride. Using this reagent it was possible to trap one of the

intermediate aziridinyll anions with certain electrophiles, whereas in all the experiments employing other sources of fluoride, protonation of the intermediate had occurred.

None of the procedures employed were successful in desilylating 1-carboethoxy-2-trimethylsilylaziridine. It was thought that this was due to the aziridine being truly unreactive (the possibility that the sources of fluoride were not nucleophilic enough, i.e., not dry enough, could not be ruled out however). It was considered that further activation in the aziridine structure would be required for more facile fluorodesilylation. Dubuffet and co-workers<sup>31</sup> have shown that 2-fluoro-2-silyloxiranes can be desilylated with relative ease. This is probably due to the stabilizing inductive effect of the  $\alpha$ -fluoride. A similar effect is likely to occur when a silylaziridine possesses an ester substituent  $\alpha$  to the silyl group. An aziridine having such a functional group is 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine, [4.4]. This compound was already being used in the current work as an aziridine that might be activated towards ring opening, particularly nucleophilic ring opening. In this latter case, it was considered that the ester group would stabilize negative charge build up in the transition state for ring opening. Most of the methods that had been employed with 1-carboethoxy-2-trimethylsilylaziridine, [4.3] were repeated with this new aziridine in the presence of a selection of electrophiles. Almost all methods led to desilylation of the aziridine. Rigorously anhydrous conditions did not appear to be necessary for the desilylation reaction; both tetrabutylammonium fluoride trihydrate and a 1M tetrabutylammonium fluoride solution in THF containing 5% water, were effective desilylating reagents. Cesium fluoride and potassium fluoride also acted as desilylating agents, but longer reaction times (overnight) were required, and reactions did not go to completion. Mixtures of products were obtained in most cases and the product mixtures were difficult to purify because of decomposition, or difficult to analyse because of the triethylsilyl group which dominates the proton NMR spectrum. In no case, however, was it possible to add electrophiles to this aziridine. It was then thought that perhaps a more activated aziridine would be one containing a methyldiphenyl or dimethylphenylsilyl group (such as [4.5]), rather than a triethylsilyl group. The diphenylmethylsilyl analogue was



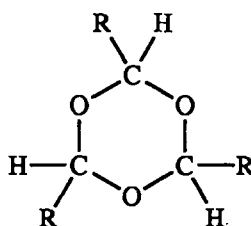
difficult to prepare and isolate but the dimethylphenylsilylaziridine [4.5], could be prepared in a pure form. It was believed that the electron-withdrawing phenyl group on the silicon would make the silicon atom more electrophilic. This would make the aziridine more activated towards desilylation. In addition the product mixtures would be more easy to analyse by  $^1\text{H}$  NMR spectroscopy than would the triethylsilyl analogues. Subsequent to completing the work for this study we found an example in the literature<sup>32</sup> which showed that a phenyl group attached to silicon promoted desilylation. In that case, replacement of a trimethylsilyl group with a dimethylphenylsilyl group in vinylsilanes, rendered otherwise unreactive compounds reactive in desilylation reactions using tetrabutylammonium fluoride (Equation 4.5).



Equation 4.5

Indeed the reactions went much more smoothly and quickly with our dimethylphenylsilylaziridine, [4.5]. Fluorodesilylation went to completion using most of the methods and the product could be readily identified and purified. Most methods however, failed to allow successful addition of electrophile and the mandatory requirement for anhydrous conditions became apparent. All the solvents had been dried, distilled, and stored over molecular sieves. The electrophiles had been purified appropriately, dried and distilled and glassware had been substituted with small teflon sealed vials. It seemed reasonable to assume that any moisture that was interfering with the reaction to cause protonation of the intermediate, must be associated with the fluoride itself. Cesium or potassium fluoride which had been heated to 200 °C for several hours when used in the reaction, still led to protonation, probably due to uptake of water on transferral to the reaction vial. Tetrabutylammonium fluoride dried by the method of Cox<sup>17</sup>, previously thought to be the most effective drying method for this compound, still led to a protonated

product. A new method was then developed for drying the tetrabutylammonium fluoride. A 10 cm<sup>3</sup> teflon sealed vial was partially filled with 4Å molecular sieves which had been dried by heating for 1 day in an oven at 200 °C and then in a vacuum oven at 90 °C for three days. The vial was then filled with commercially prepared 1.0M tetrabutylammonium fluoride in THF containing 5% water. After several hours shaking the liquid was quickly transferred into a second vial containing fresh, activated molecular sieves and shaken for 24 hours. The preparation was used within the next 24 hours. Before the reaction, the vacuum dried aziridine was weighed (typically 0.1 g) into a small reaction vial which was then sealed and flushed with dry nitrogen. The electrophile was then introduced by syringe and the vial swirled or warmed until the layers were mixed. The vial was then cooled and a catalytic amount of the tetrabutylammonium fluoride solution was added followed by 0.5 cm<sup>3</sup> of dry THF. Deviation from this procedure gave poorer results. Hexanal and benzaldehyde gave addition products in good yield but no ketones could be added. Even cyclohexanone, which is more electrophilic than most ketones due to lack of steric hindrance, failed to add under these conditions. Similarly, pivaldehyde could not be added, probably due to steric effects. Aldehydes such as acetaldehyde and propionaldehyde which possess an  $\alpha$ -hydrogen also, did not undergo addition but underwent trimerization (as below), the desilylated protonated aziridine being formed as well. (Hexanal was an exception to this rule however.)



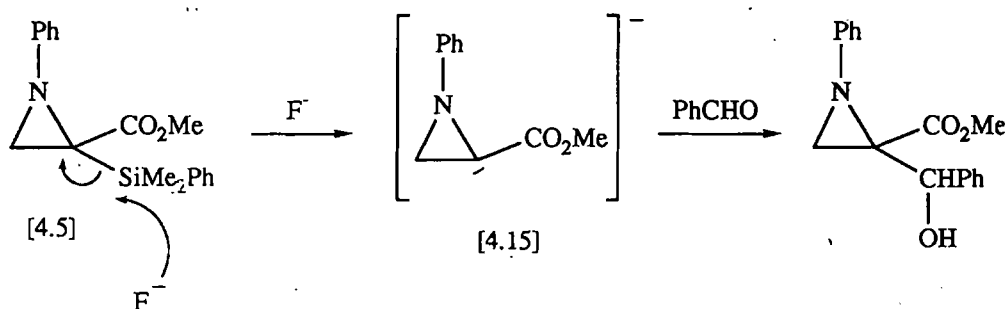
Trimer from aldehyde polymerization

There later emerged evidence that in these cases the aziridinyll anion, acting as a strong base abstracts a proton from the aldehyde initiating an aldol type reaction resulting in the formation of the trimeric products just described.

The products formed from hexanal and benzaldehyde were obtained in good yield and purified by column chromatography. In fact, the silyl ethers were isolated and the silyl groups could not be removed even by adding more tetrabutylammonium fluoride solution. Whereas the reaction with benzaldehyde led almost quantitatively to the formation of the corresponding silyl ether (along with a small amount of the free alcohol), the reaction with hexanal led to a mixture consisting mainly of the free alcohol and a small amount of the silyl ether. Since in both cases, only the silyl ethers could be retrieved from the column, the overall yield of the product from hexanal was rather low. An NMR study of the products in DMSO showed that the silyl ether was present as a mixture of diastereoisomers in roughly equal amounts.

#### 4.5 Mechanism of fluorodesilylation of silylaziridines

There are at least two plausible mechanisms for the desilylation reaction. In one case, the fluoride ion attacks at silicon and the aziridinyl anion, [4.15], is displaced in an  $S_N2$  type mechanism. The anion is then subject to attack by an electrophile (Scheme 4.3).



Scheme 4.3

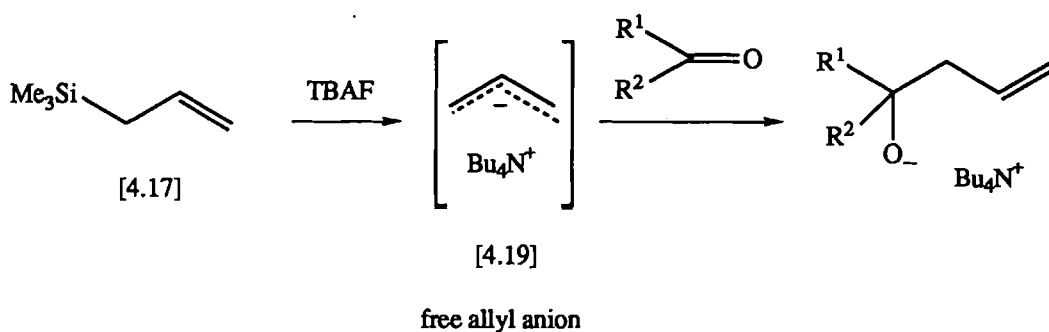
In the second mechanism, nucleophilic attack by fluoride could lead to a discrete penta-coordinate intermediate, [4.16].



Majetich and co-workers<sup>33</sup> have proposed that in an allylation procedure using allyltrimethylsilane, [4.17] and a catalytic amount of fluoride (tetrabutylammonium fluoride), the nucleophilic species involved is a non basic penta-coordinate silicon intermediate, [4.18] resulting from fluoride ion addition (Equation 4.6).

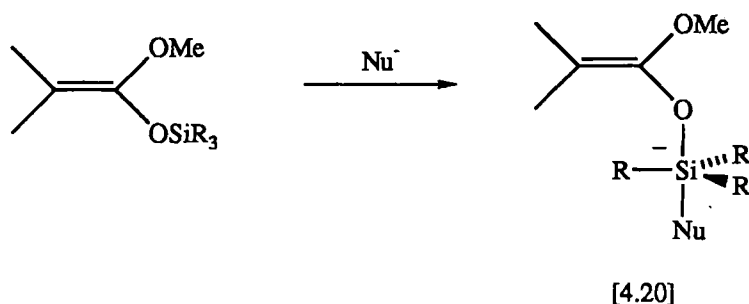


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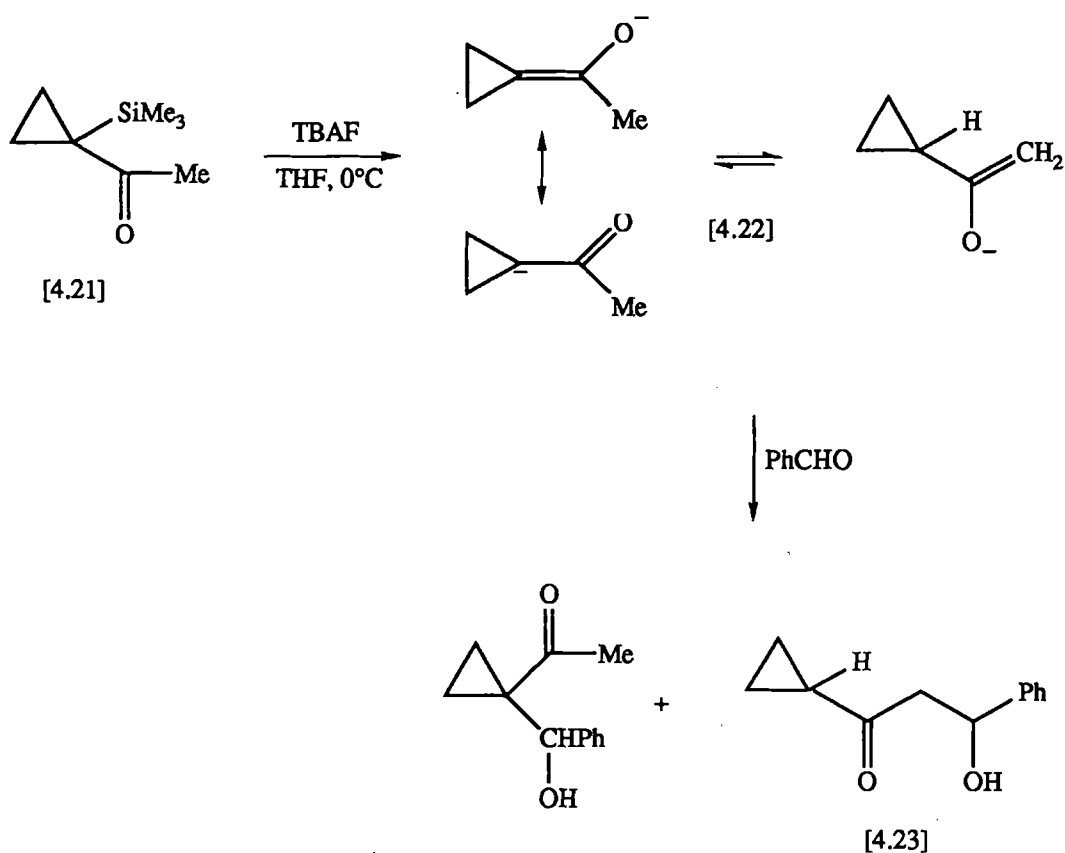
Scheme 4.6

Sakurai<sup>35</sup> later proposed that a mechanism involving a hypervalent silicon species, [4.20] is possible in methyl methacrylate group transfer polymerization reactions (Equation 4.7).



Equation 4.7

There is no clear evidence to support either of these two mechanisms exclusively. There are some lines of evidence which support both theories and further studies are required to be more certain of the mechanistic aspects of the reaction. Formation of the naked anion on a three membered ring is expected to be more difficult than the same reaction in an acyclic analogue. This is due to the constraints imposed by the ring. The anion is stabilized by field effects offered by the ester group, but stabilization by resonance with the substituent may be minimal since this requires the adoption of a planar structure which is impeded by the small angle required for the three membered ring.

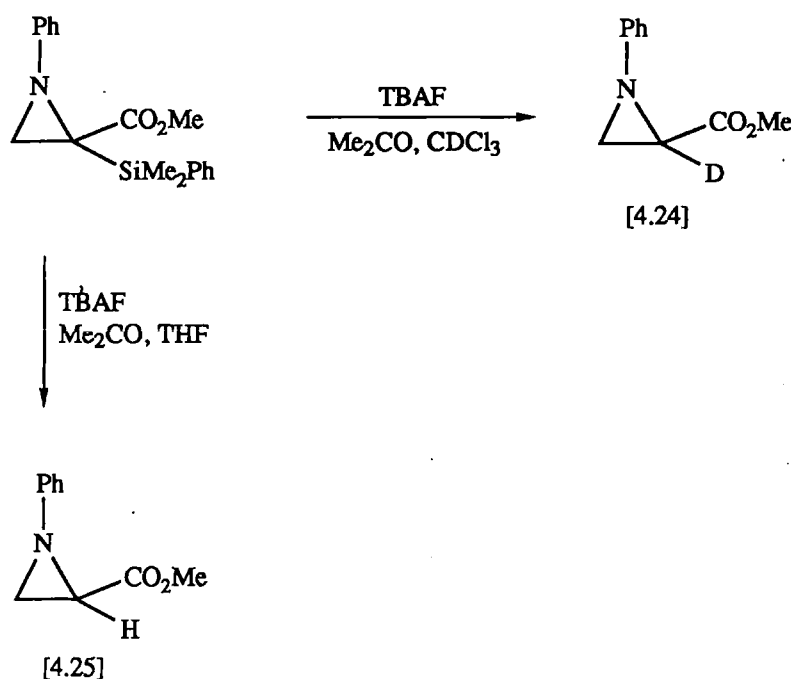


Scheme 4.7

However, Paquette<sup>36</sup> has shown that an enolate anion, [4.22] is an intermediate in the reaction of 1-trimethylsilylcyclopropanemethyl ketone, [4.21] with fluoride ion and aldehydes (Scheme 4.7). If the reaction proceeded by a penta-coordinate intermediate in this case, the  $\beta$ -keto alcohol, [4.23] would not have been isolated. However, this does not prove that appreciable amounts of the enolate rather than the cyclopropyl anion were involved. In the current study, the aziridine having the triethylsilyl group, [4.4] rather than the dimethylphenylsilyl group, [4.5] desilylated, albeit sluggishly, yet failed to react subsequently with electrophiles. If a naked enolate were the reactive intermediate, this would be the same in both cases and both aziridines should lead to the same product. The fact that one aziridine was capable of adding electrophiles, whereas the other always led to the protonated product, suggests that a silicon species is still involved in the electrophilic capture step. This supports a mechanism where both aziridines form a penta-coordinate intermediate, but the approach of the electrophile is sterically hindered in the case of the

triethylsilyl substituted aziridine, resulting in eventual protonation by abstraction from solvent, or by water on work-up.

There is one observation however which is inconsistent with the above mechanism. A reaction was carried out in an NMR tube using 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine [4.5] and a catalytic amount of molecular sieve dried tetrabutylammonium fluoride in the presence of acetone, with deuteriochloroform as the solvent. A highly significant result was obtained. When the same experiment was carried out in THF the desilylated, protonated aziridine [4.25] was formed quantitatively. However, in the former case, the desilylated deuterated aziridine [4.24] was formed exclusively (Scheme 4.8).

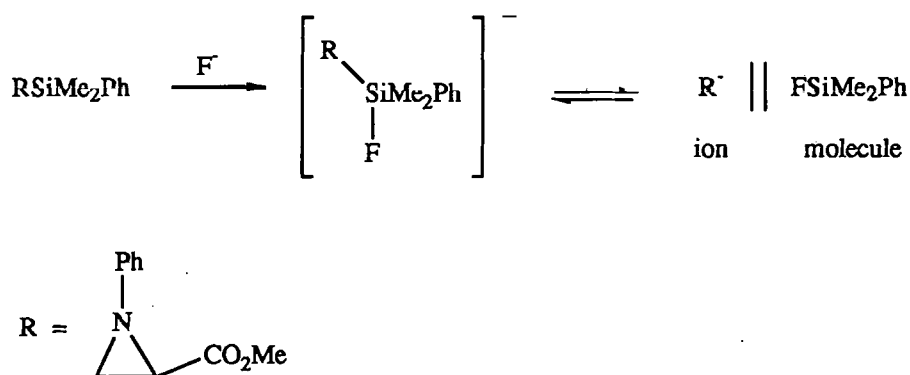


**Scheme 4.8**

This result is of major importance as it demonstrates that the intermediate must be significantly basic in order to abstract a deuterium atom from deuteriochloroform, in particular, in competition between deuteriochloroform and acetone. In this situation the aziridinyl anion (or equivalent), proves to be more basic than nucleophilic. It may be, as was mentioned earlier, that the intermediate, acting as a strong base, is responsible for

initiating an aldol reaction with some of the aldehydes used. The fact that the intermediate is quite so basic tends to disfavour a mechanism whereby an electrophile (or proton) reacts by donation of a carbon-silicon bond in a hypervalent silicon species.

One mechanism which is consistent with most of the observations does not involve a true penta-coordinate silicon species, but involves a loosely associated ion-molecule pair of the fluorosilane and the aziridinyll anion (Scheme 4.9).



Scheme 4.9

Such a mechanism would account for the basicity of the intermediate and the failure of the triethylsilyl substituted aziridine to react with electrophiles. It is also in agreement with the suggestion that the anion is responsible for abstracting protons from some of the aldehyde which results in trimerization. Further studies are required, however, in order to determine which mechanism is in operation.

In summary, all but one of the observations could support a mechanism involving an essentially naked carbanion. However, if this were the case, then both of the aziridines which desilylated, should also add electrophiles. A fully penta-coordinate intermediate is not supported by the observation of the intermediate acting as a strong base. A mechanism which fits with all of the observations however, involves a loosely associated ion-molecule pair.



## 4.6 Spectroscopic Features

All of the desilylated products were fully characterised using  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy. The data are given in Table 4.1. There are several interesting features of the spectra.

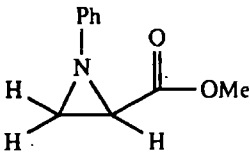
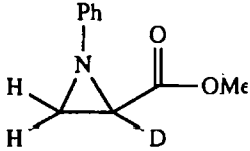
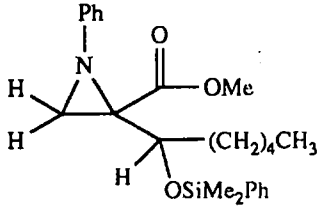
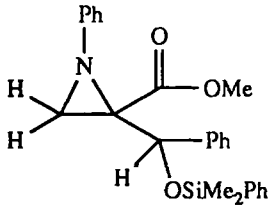
The spectra for the desilylated, protonated aziridine [4.25], are fairly typical. In the  $^1\text{H}$  NMR spectrum, three sets of doublets of doublets are observed for the three ring protons. The deuterated aziridine, [4.24] could easily be identified by comparing its spectra with those of the protonated analogue. The  $^{13}\text{C}$  NMR spectrum is almost identical to that of [4.25], however, the CD resonance is a 1:1:1 triplet due to deuterium coupling. Several differences occur in the  $^1\text{H}$  NMR spectrum. The two ring protons resonate as two singlets, i.e., the geminal coupling constant is zero and these protons are not coupled to any other protons. The remainder of the spectrum is similar to that of [4.25] (with the absence of the resonance at 2.26 ppm), strongly supporting the suggested structure.

Interestingly, in the case of the two products [4.1a] and [4.1b], resulting from an electrophilic capture of hexanal and benzaldehyde, the product mixtures are shown to be diastereoisomeric. This is due to the presence of two chiral carbon sites in the molecule, one being the fully substituted ring carbon and the other, the adjacent silyl ether carbon. In the case of [4.1b], the adduct with benzaldehyde, both the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra show a mixture of diastereoisomers present in roughly equal amounts. In the  $^1\text{H}$  NMR spectrum two 6 H high field singlet resonances are observed corresponding to the methyl groups attached to the silicon atom. Although theoretically there should be four environments for the four sets of silicon methyl protons, only two are observed owing to accidental equivalence either between the diastereoisomers or between the two methyl groups in each diastereoisomer. As discussed later, these four different environments are detected in the  $^{13}\text{C}$  NMR spectrum. Two singlets are observed corresponding to the two diastereoisomeric ring  $\text{CH}_2$  groups. No geminal coupling is observed between the two protons in each isomer in deuteriochloroform. Two sets of resonances are observed for the

methyl ester protons and also for the single proton on the carbon bearing the silyl ether. Similarly, two resonances are observed for each carbon atom in the  $^{13}\text{C}$  NMR spectrum. These correspond to the two diastereoisomers. In this case four distinct environments are observed for the silyl methyl carbons.

A similar situation is observed when hexanal was employed. However, in this case, as expected for two diastereoisomers, four distinct proton environments are observed for the silyl methyl groups, but only two carbon environments. The  $^1\text{H}$  NMR spectrum again shows one set of resonances for each diastereoisomer. However, the two diastereoisomers are not differentiated by  $^{13}\text{C}$  NMR.

Table 4.1 NMR Spectroscopic data<sup>1</sup>

Entry	NMR Data
 [4.25]	<sup>1</sup> H (CDCl <sub>3</sub> ) 2.26 (1 H, dd, <i>J</i> 1.46 Hz and 6.34 Hz, CHCO <sub>2</sub> Me), 2.63 (1 H, dd, <i>J</i> 1.46 Hz and 2.91 Hz, NCH <sub>2</sub> H <sub>b</sub> ), 2.76 (1 H, dd, <i>J</i> 6.34 Hz and 2.91 Hz, NCH <sub>2</sub> H <sub>b</sub> ), 3.74 (OCH <sub>3</sub> ), 6.88-7.55 (5 H, m, Ph).  <sup>13</sup> C 33.7 (CH <sub>2</sub> ), 37.5 (CH), 52.1 (OCH <sub>3</sub> ), 120.7, 123.4, 129.1 and 152.5 (Ph), 170.5 (C=O).
 [4.24]	<sup>1</sup> H 2.24 (1 H, s, CH <sub>2</sub> H <sub>b</sub> ), 2.60 (1 H, s, CH <sub>2</sub> H <sub>b</sub> ), 3.76 (OCH <sub>3</sub> ), 6.79-7.55 (5 H, m, Ph).  <sup>13</sup> C 34.4 (CH <sub>2</sub> ), 38.1 (1:1:1 triplet, CD), 53.1 (OCH <sub>3</sub> ), 121.6, 124.0, 129.5 and 152.5 (Ph), 170.1 (C=O).
 [4.1a] <sup>2</sup>	<sup>1</sup> H 0.313, 0.335, 0.339, 0.358 (4 x 3 H, 4 x s, Me <sub>2</sub> Si), 0.78-0.82 (3 H, 2 overlapping triplets, CH <sub>2</sub> Me <sub>x</sub> and CH <sub>2</sub> Me <sub>y</sub> ), 1.20-1.66 (8 H, m, CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> ), 2.28 and 2.57 (1 H, 2 x d, <i>J</i> 1.6 Hz, H <sub>xa</sub> and H <sub>xb</sub> ), 2.51 and 2.64 (1 H, 2 x d, <i>J</i> 2.0 Hz, H <sub>ya</sub> and H <sub>yb</sub> ), 3.18 and 3.28 (3 H 2 x s, OMe <sub>y</sub> and OMe <sub>x</sub> ), 4.14 and 4.38 (1 H, 2 x dd, <i>J</i> <sub>1x</sub> 5.8, <i>J</i> <sub>2x</sub> 8.4, <i>J</i> <sub>1y</sub> 3.2, <i>J</i> <sub>2y</sub> 8.0 Hz, HCOSi), 6.62-7.58 (10 H, m, PhN and PhSi).  <sup>13</sup> C -0.6, -0.2 (SiMe <sub>2</sub> ), 14.7 (CH <sub>3</sub> ), 23.3 (CH <sub>3</sub> CH <sub>2</sub> ), 26.3 (CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> ), 32.4 (CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> ), 34.1 (SiOCH <sub>2</sub> CH <sub>2</sub> ), 35.2 (NCH <sub>2</sub> ), 51.2 (CH <sub>3</sub> O), 52.3 (COC <sub>2</sub> Me), 72.2 (COSi).
 [4.1b] <sup>1</sup>	<sup>1</sup> H 0.29 and 0.32 (2 x 3H, 2 x s, Me <sub>2</sub> Si), 2.49 and 2.73 (2 H, 2 x s, H <sub>2</sub> C <sub>x</sub> and H <sub>2</sub> C <sub>y</sub> ), 3.28 and 3.31 (3 H, 2 x s, OMe <sub>x</sub> and OMe <sub>y</sub> ), 5.34 and 5.60 (1 H, 2 x s, PhCH <sub>x</sub> and PhCH <sub>y</sub> ), 6.64-7.91 (15 H, m, NPh, CPh, SiPh).  <sup>13</sup> C -0.85, -0.33, -0.32, 1.7 (4 x CH <sub>3</sub> , SiMe), 34.5 (H <sub>2</sub> C <sub>y</sub> ), 34.7 (H <sub>2</sub> C <sub>x</sub> ), 51.7, 51.8, 52.2 and 52.3 (OMe <sub>x&amp;y</sub> and MeOCOC <sub>x&amp;y</sub> ), 120.2-141.7 (14 resonances, NPh, CPh, SiPh), 150.2 and 150.7 (2 x ipso C from NPh), 168.7 and 169.1 (MeOCOC <sub>x&amp;y</sub> ).

<sup>1</sup>All of the spectra were recorded on a 400 Mz instrument.<sup>2</sup>The two diastereoisomers are denoted with x and y subscripts.

## 4.7 Conclusions

In general, tetrabutylammonium fluoride is a superior desilylating agent compared with alkali metal fluorides such as potassium or cesium fluoride. The nucleophilicity of the fluoride ion in tetrabutylammonium fluoride is increased when water is absent from the system, although water can be tolerated when the silyl species is highly reactive towards fluoride ion. The best method of drying this source of fluoride was found to involve the treatment of a (5% aqueous) 1M THF solution with molecular sieves.

A phenyl group on the nitrogen and /or an ester substituent in the 2-position in silylaziridines has an activating effect towards fluorodesilylation. There is evidence that stabilizing substituents in the 2-position have a greater effect than those in the 1-position. A phenyl group on the silicon atom in a silylaziridine seems to enhance its reactivity towards fluorodesilylation.

The most likely mechanism for fluorodesilylation, at least in the systems studied here, is one involving not a 'naked' anion or a true hypervalent silicon intermediate, but a loosely associated ion-molecule pair. The bulk of the silyl group therefore has the effect of sterically deflecting electrophiles present in a fluorodesilylation reaction. The desilylated intermediates in the reactions studied are remarkably basic. As a result, only powerful electrophiles can be used in the reaction otherwise the reactive intermediate reacts as a base rather than a nucleophile. However, very powerful electrophiles such as methyl iodide, react preferentially with the fluoride ion thus preventing desilylation.

#### 4.8 References

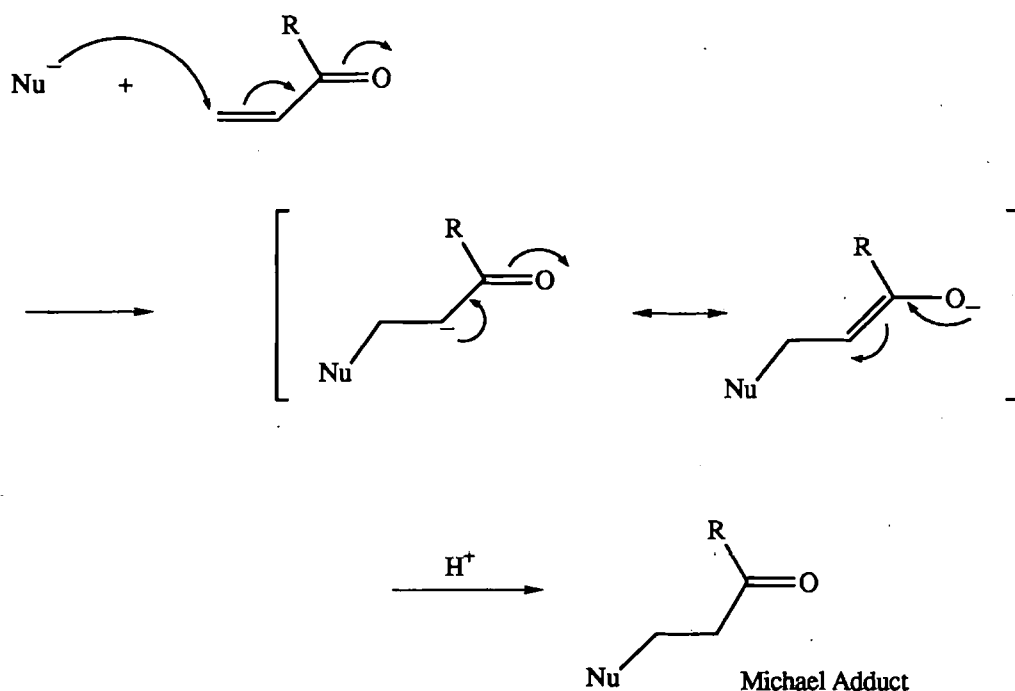
1. T.H. Chan, P.W.K. Lau and M.P. Li, *Tetrahedron Lett.*, 2667, (1976).
2. E.A.V. Ebsworth in "Organometallic Compounds of the Group IV Elements", Ed., A.G. MacDiarmid, Marcel Dekker, New York, 1968, p. 46.
3. J.H. Clark, *Chem. Rev.*, 429, (1980).
4. R.K. Sharma and J.L. Fry, *J. Org. Chem.*, **48**, 2112, (1983).
5. J.H. Clark and J.M. Miller, *J. Am. Chem. Soc.*, **99**, 498, (1977).
6. J. Emsley, O.P.A. Hoyte and R.E. Overill, *J. Chem.Soc., Chem. Commun.*, 225, (1977).
7. G. Majetich, R.W. Desmond, Jr., and J.J. Soria, *J. Org. Chem.*, **51**, 1753, (1986).
8. J.H. Clark, and J.M. Miller, *J. Chem. Soc., Perkin 1*, 2063, (1977).
9. T.H. Chan, and W. Mychajlowskji, *Tetrahedron Lett.*, 171, (1974).
10. R.F. Cunico and E.M. Dexheimer, *J. Am. Chem. Soc.*, **94**, 2868, (1972).
11. J.H. Clark, and J.M. Miller *J. Chem. Soc., Perkin 1*, 1743, (1977).
12. J.W. Middleton, U.S. Patent 3940402, 1976.
13. R. Noyori, I. Nishida and J. Sakata, *J. Am. Chem. Soc.*, **105**, 1598, (1983).
14. R.S. Atkinson and B.J. Kelly, *Tetrahedron Lett.*, 2703, (1989).
15. M.C.C. Soobramanien, Ph.D. Thesis, The Open University, Milton Keynes, (1988).
16. R.S. Atkinson and B.J. Kelly, *J. Chem. Soc., Perkin 1*, 1657, (1989).
17. D.P. Cox, J. Terpinski and W. Lawrynowicz, *J. Org. Chem.*, **49**, 3216, (1984).
18. T.H. Chan and W. Mychajlowskij, *Tetrahedron Lett.*, 3479, (1974).
19. J.J. Berzelius, *Traite de Chemie*, **1**, 553, (1838).
20. G.G. Yakobson. and N.E. Akhmetova, *Synthesis*, **3**, 169, (1983).
21. C.L. Liotta and H.P. Harris, *J. Am. Chem. Soc.*, **96**, 2250, (1974).
22. M. Gingras and D.N. Harpp, *Tetrahedron Lett.*, 4669, (1988).
23. J.H. Clark and D.J. Macquarrie, *Tetrahedron Lett.*, 111, (1987).

24. E.F. Westrum Jr. and K.S. Pitzer, *J. Am. Chem. Soc.*, **71**, 1940, (1949).
25. E.F. Westrum Jr. and G.A. Burney, *J. Phys. Chem.*, **65**, 344, (1961).
26. J.H. Clark and J.M. Miller, *Can. J. Chem.*, **56**, 141, (1978).
27. A. Terenin and V. Filimonov, in "Hydrogen Bonding", Ed. D. Hadzi, Pergamon, London, 1959.
28. J.H. Clark, *J. Chem. Soc., Chem. Commun.*, 789, (1978).
29. I. Kuwajima, E. Nakamura, and M. Shimizu, *J. Am. Chem. Soc.*, **104**, 1025, (1982).
30. M. Gingras, T.H. Chan and D.N. Harpp, *J. Org. Chem.*, **55**, 2078, (1990).
31. T. Dubuffet, R. Sauvêtre, and J.F. Normant, *Tetrahedron Lett.*, **29**, 5923, (1988).
32. H. Oda, M. Sato, Y. Morizawa, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, 2877, (1983).
33. G. Majetich, A. Casares, D. Chapman, and M. Behnke, *J. Org. Chem.*, **51**, 1745, (1986).
34. A. Hosomi, A. Shirhata and H. Sakurai, *Tetrahedron Lett.*, 3043, (1978).
35. H. Sakurai, "Organosilicon and Bioorganosilicon Chemistry: Structure, Bonding, Reactivity, and Synthetic Application", Ellis Horwood, 1985, p 222.
36. L.A. Paquette, C. Blankenship, and G.J. Well, *J. Am. Chem. Soc.*, **106**, 6442, (1984).

## CONJUGATE ADDITION REACTIONS OF SOME VINYLSILANES

### 5.1 Introduction

Conjugate addition, the 1,4-addition of a nucleophile to a conjugated system represents a valuable method of extending a carbon chain. When the conjugated system is an  $\alpha,\beta$ -unsaturated carbonyl compound, and the nucleophile is an enolate, the reaction is known as the Michael reaction<sup>1</sup> (Scheme 5.1). More recently the term has also come to include other 1,4 additions to  $\alpha,\beta$ -unsaturated carbonyl compounds.

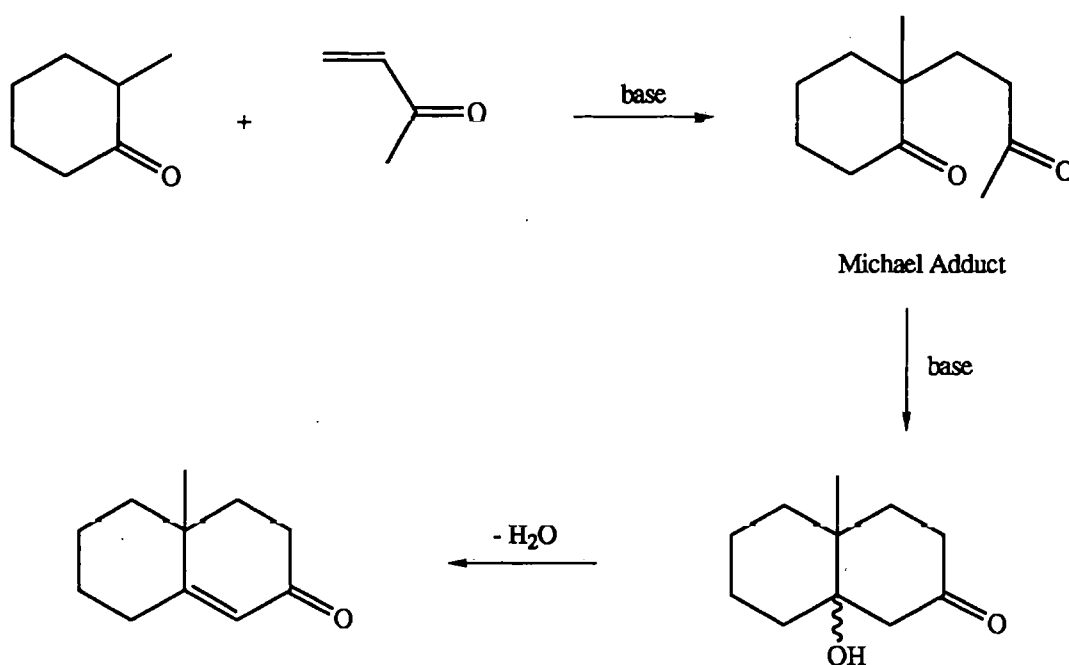


Scheme 5.1 The Michael Reaction

Although it is one of the most widely used methods of carbon-carbon bond formation, the Michael reaction is often complicated by polymerization of the  $\alpha,\beta$ -unsaturated carbonyl

compound, poor regioselectivity, reverse Michael reactions, and self condensation of enolate products. In the current work, although the initial findings were by chance, some of these problems have been eliminated, as will be discussed later.

One form of the Michael reaction, the Robinson annulation<sup>2</sup> (Scheme 5.2), which is effectively a Michael reaction followed by an aldol condensation, is often associated with some of the problems previously mentioned.



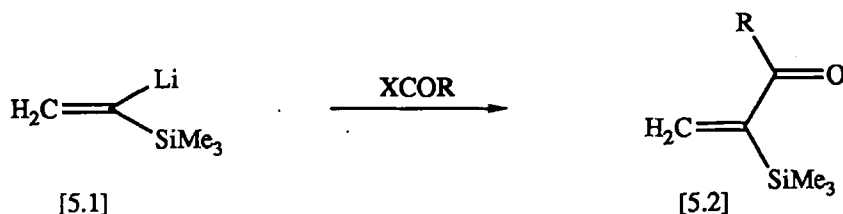
Scheme 5.2 Robinson annulation

#### 5.1.1 Initial aims of the project

The work presented in this Chapter opens up an interesting new field of study which in some respects deviates from the more central theme of the thesis which concerns silylaziridines. Nonetheless, the findings are significant and the initial results although unexpected, demanded further investigation. The initial aims of the project which eventually evolved had been to prepare functionalized vinylsilanes which would be used as intermediates in silylaziridine synthesis. It had been hoped that under suitable conditions



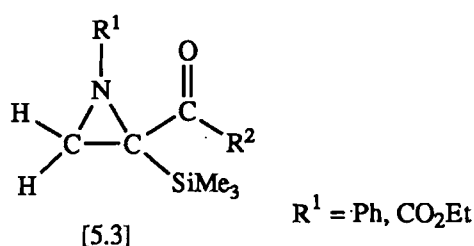
the reaction of  $\alpha$ -lithiovinyltrimethylsilane [5.1] with appropriate electrophiles would provide a facile, one-step route to  $\alpha$ -carbonylvinylsilanes [5.2] as shown in Equation 5.1.



Equation 5.1

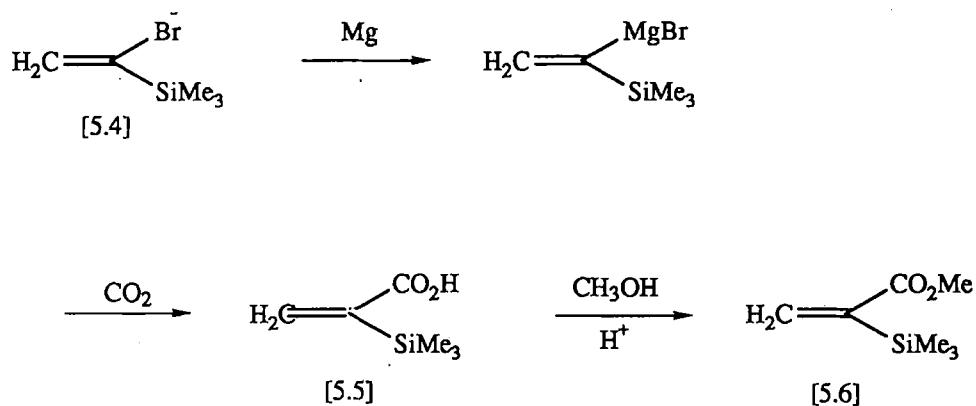
However, the desired products were not isolated as they underwent further reaction by Michael addition with the starting materials. These findings were considered to be highly significant and so a fuller study was undertaken. The material presented here concerns the Michael addition reactions of  $\alpha$ -lithiovinyltrimethylsilane with a series of  $\alpha$ -carbonylvinylsilanes. Different reactivities were observed in each case leading to a range of new compounds.

$\alpha$ -Carbonylvinylsilanes, e.g. [5.2], represent valuable synthetic intermediates since both substituents are capable of stabilizing a negative charge in the  $\alpha$ -position.



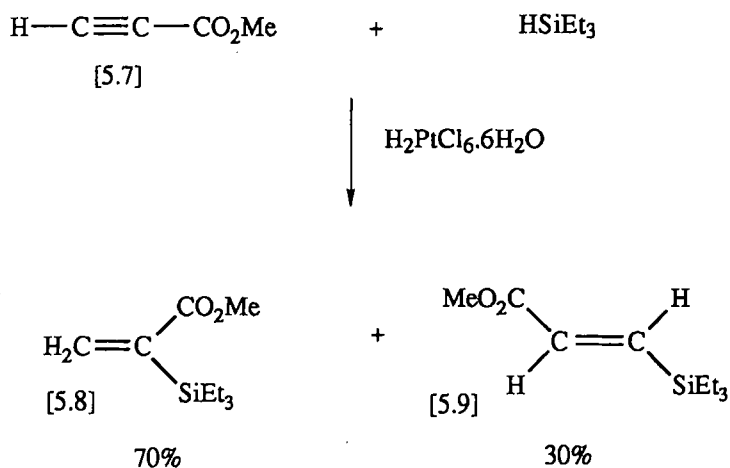
Such vinylsilanes should be effective precursors to activated aziridines of the type [5.3], either by thermolysis of phenyl azide; or photolysis of ethyl azidoformate, in the presence of the vinylsilane. The vinylsilanes initially targeted were the  $\alpha$ -methyl or ethyl trimethylsilylpropenoates and it was hoped that the reaction of  $\alpha$ -lithiovinyltrimethylsilane, [5.1] with methyl and ethyl chloroformate would provide a facile new one step route to these compounds. The preparation of methyl 2-trimethylsilylpropenoate, [5.6] is reported

in the literature<sup>3</sup>, but unfortunately, it involves a three step reaction from  $\alpha$ -bromovinyltrimethylsilane, [5.4]. The 2-trimethylsilylpropenoic acid, [5.5], prepared by carbonation of the Grignard reagent, is subsequently methylated with acidic methanol yielding the ester, [5.6] (Scheme 5.3).



Scheme 5.3

Another route<sup>4</sup> is available for the preparation of methyl 2-triethylsilylpropenoate [5.8] via hydrosilylation of methyl propynoate [5.7] leading to a mixture of regioisomers [5.8] and [5.9], which then have to be separated (Equation 5.2).



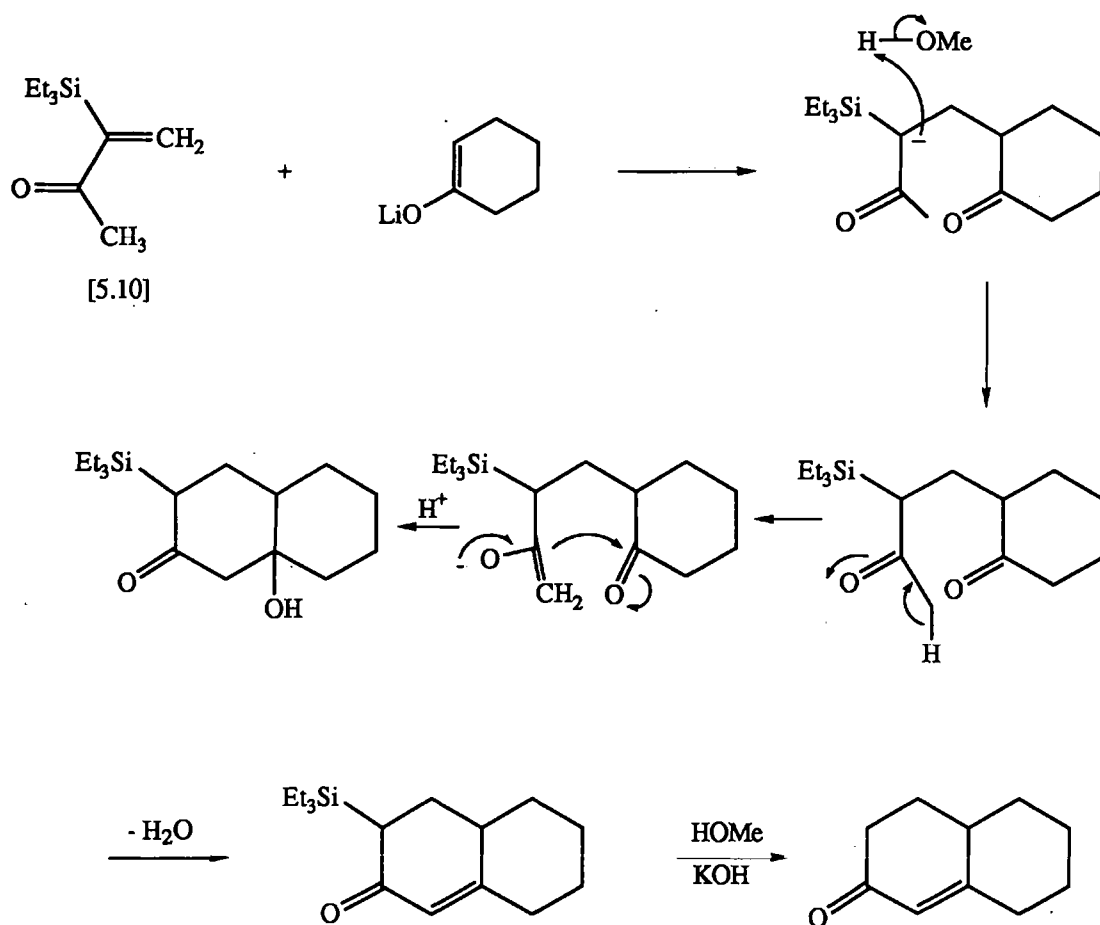
Equation 5.2

However, this route is not easily accessible for the trimethylsilyl analogue since the hydrosilylating agent is gaseous at ambient temperature.

The first reaction attempted in the current work was the synthesis of ethyl 2-trimethylsilylpropenoate. It was found that the desired product underwent Michael addition with the starting material which prompted us to investigate the reaction using other electrophiles and the results are reported below.

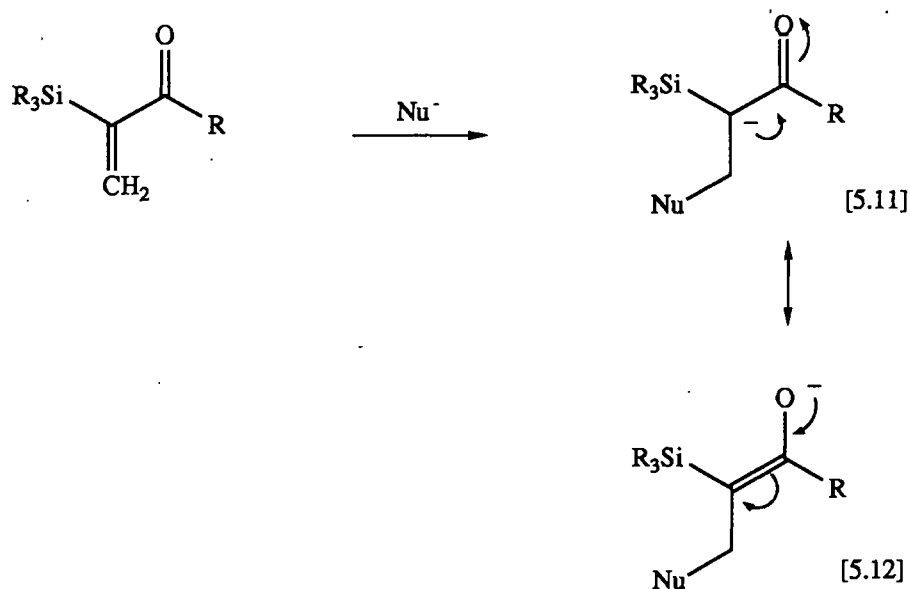
## 5.2 The role of silicon in promoting the Michael reaction

Stork<sup>5</sup> was the first to exploit the silicon moiety as an easily removed stabilizing group in such reactions (Scheme 5.4).



**Scheme 5.4**

The advantages of using an  $\alpha$ -silyl substituted vinylketone (such as [5.10]) in the reaction were found to be several-fold. With simple vinylketones the base strengths and reactivities of the enolate ions derived from the starting material and the adduct can be similar, resulting in low yields of product. However, introducing a silicon group at the  $\alpha$ -position stabilizes the enolate intermediate, shifting the equilibrium in favour of the products (Scheme 5.5). The carbanionic resonance form, [5.11] is stabilized<sup>6</sup> to a greater extent than the enolate form, [5.12] therefore reducing the reversibility of the reaction.



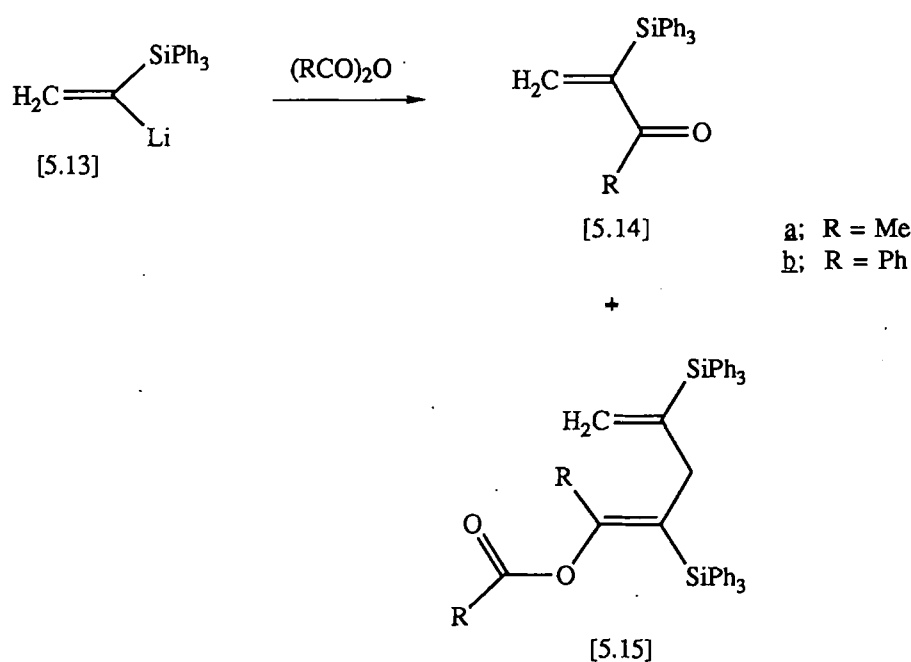
Scheme 5.5

Since silylenones are so reactive in Michael addition reactions, aprotic conditions could be employed (protonation is not required to favour the products) thus minimising side reactions. While these conditions would normally favour polymerization of the vinylketone, the silicon moiety retards polymerization through steric hindrance, and probably through reduced reactivity as a result of the extra stabilization of the enolate from the  $\alpha$ -silicon. Also 1,2-addition of the enolate is disfavoured partly by steric hindrance again, but more importantly through the kinetic and thermodynamic stabilization of forming a 1,4-adduct. The silyl group is easily cleaved at the end of the reaction by heating with methanolic sodium hydroxide.

## 5.3 Previous reactions involving $\alpha$ -lithiovinyltrialkylsilanes and carbonyl compounds

### 5.3.1 General aspects of the Michael addition reaction

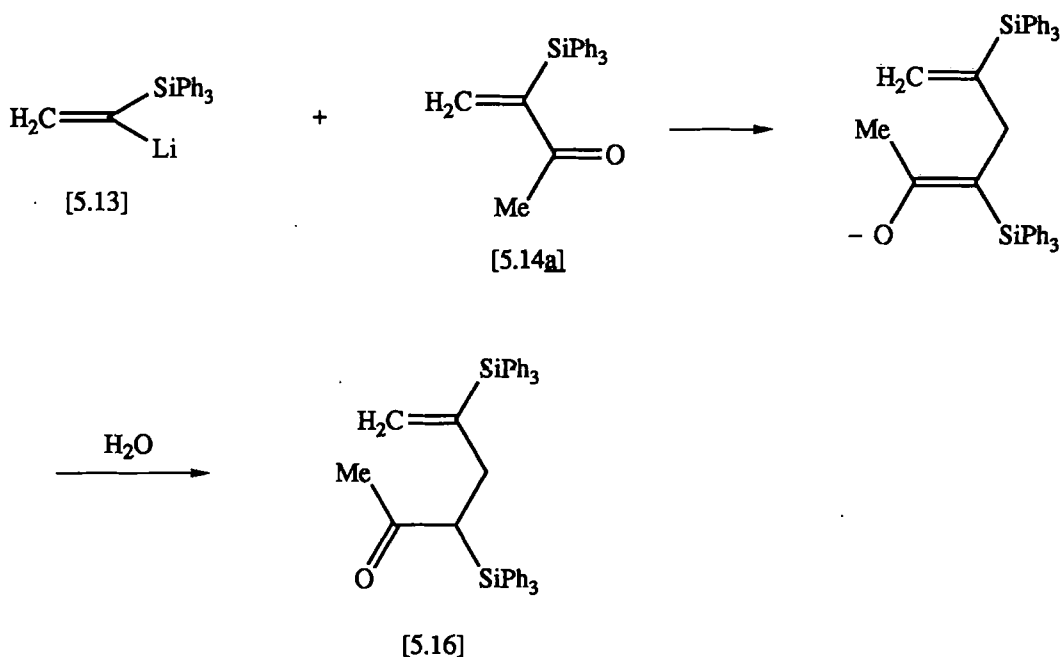
Brook and Duff<sup>7</sup> reported reactions of  $\alpha$ -lithiovinyltrialkylsilanes with activated carbonyl compounds. They described the reaction of  $\alpha$ -lithiovinyltriphenylsilane, [5.13] (Equation 5.3) and *trans*-1-lithio-2-phenyl-1-triphenylsilylene, [5.17], (Equation 5.4, overleaf) with acetic and benzoic anhydride. Two different types of product were obtained in each case.



Equation 5.3

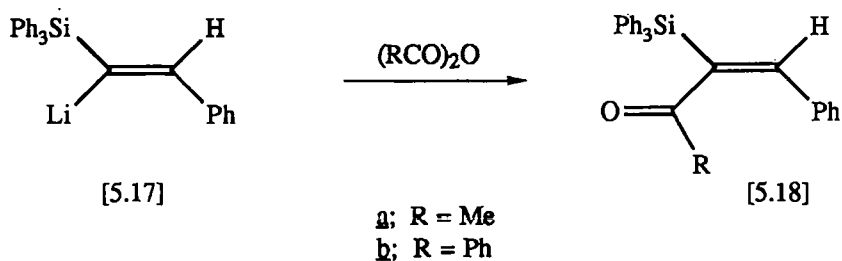
Treatment of  $\alpha$ -lithiovinyltriphenylsilane, [5.13] at room temperature with an excess of acetic anhydride afforded mainly a product of 1,4-addition, [5.15] along with a small amount of the  $\alpha,\beta$ -unsaturated ketone, [5.14a], while at  $-78^\circ C$  the vinylketone was obtained in 82% yield.

However when a sample of 3-triphenylsilylbut-3-en-2-one, [5.14a] was treated with  $\alpha$ -lithiovinyltriphenylsilane, [5.13] at  $-78\text{ }^{\circ}\text{C}$ , the Michael addition product, [5.16] was obtained in 67% yield (Scheme 5.6).



Scheme 5.6

When *trans*-1-lithio-2-phenyl-1-triphenylsilyl ethene, [5.17] was used as the donor species (at  $-78\text{ }^{\circ}\text{C}$ ) no 1,4-addition to the product vinylketones was observed (Equation 5.4). No explanation is given for this observation, however, the  $\alpha,\beta$ -unsaturated ketone, [5.18], formed in this reaction appears less likely to undergo conjugate addition on both steric and electronic grounds.

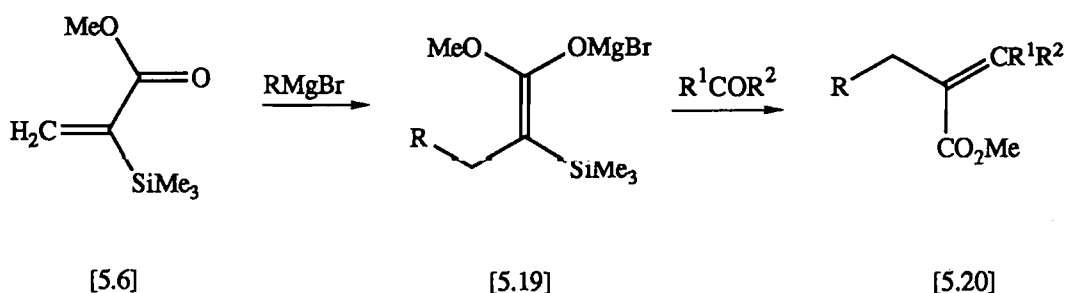


Equation 5.4

In the same publication the authors reported the reactions of anhydrides with the corresponding Grignard reagents:  $\alpha$ -trimethylsilylvinyl magnesium bromide and  $\beta$ -trimethylsilylvinyl magnesium bromide, giving similar results.

### 5.3.2 Reactions involving Michael addition-Peterson Olefination

Tsuge<sup>8</sup> and co-workers have explored the Peterson Olefination (Scheme 5.7) of the carbanions resulting from the Michael addition of organometallics to methyl 2-trimethylsilylpropenoate, [5.6]. A series of reactions were conducted in which stabilized enolates of the type [5.19] were generated by Michael addition of Grignard reagents to methyl 2-trimethylsilylpropenoate, [5.6]. These then react in good yield with aldehydes to generate Peterson Olefination products, [5.20].



Scheme 5.7

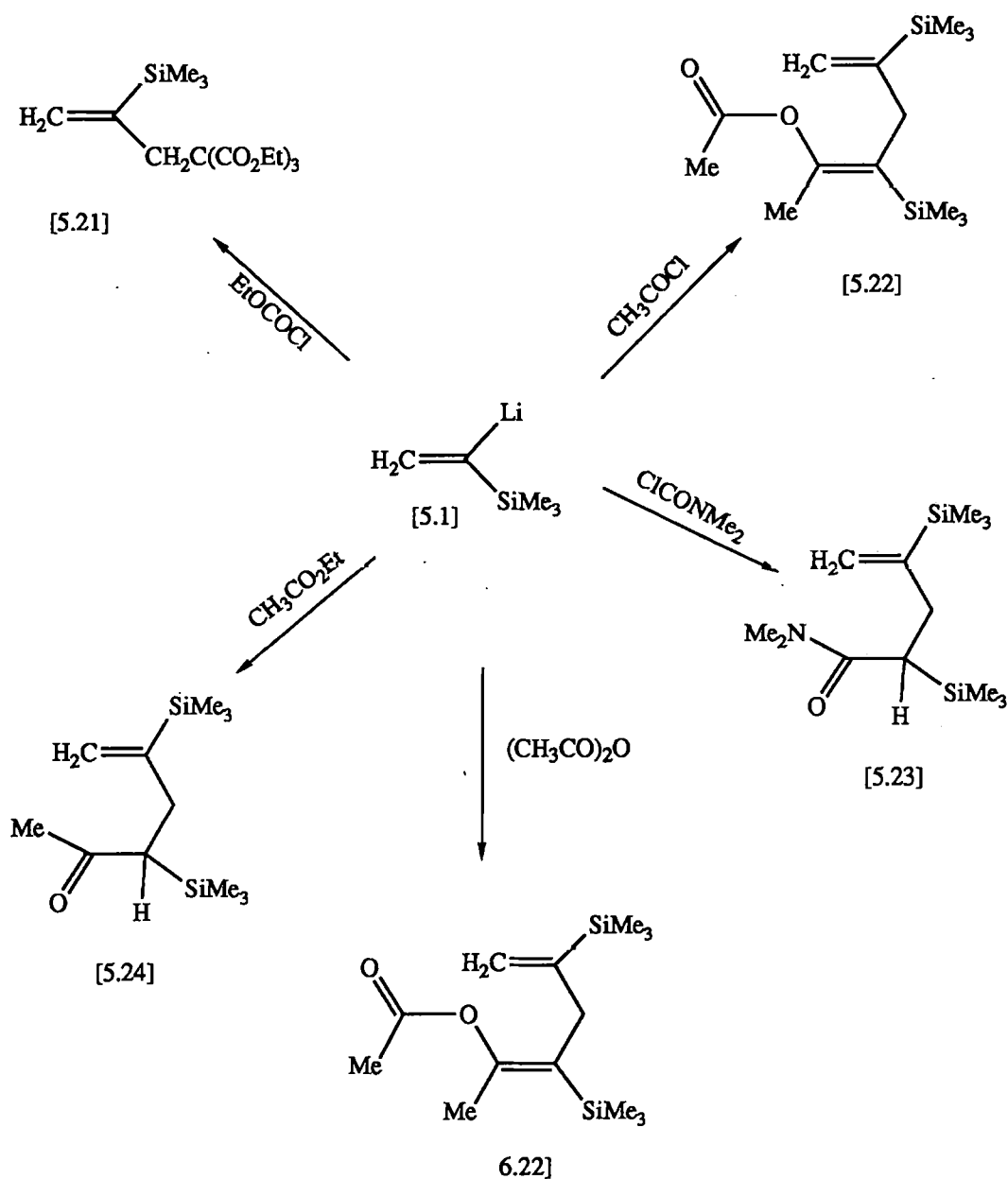
There was no evidence, however, of an intermediate enolate, [5.19], acting as a Michael donor to the starting  $\alpha,\beta$ -unsaturated carbonyl compound.

A later communication by Tsuge<sup>9</sup> however reports that the intermediate enolate can be made to undergo a further 1,4-addition when two rather than one equivalents of methyl 2-trimethylsilylpropenoate are used.

## 5.4 Experimental aspects of the Michael addition reactions

### 5.4.1 Introduction

In this project an interesting series of new compounds [5.21]–[5.24] has been produced through the reaction of  $\alpha$ -lithiovinyltrimethylsilane with a range of carbonyl compounds.



Scheme 5.8



The intermediate  $\alpha,\beta$ -unsaturated carbonyl compounds subsequently act as Michael acceptors to  $\alpha$ -lithiovinyltrimethylsilane, [5.1]. The Michael products then either undergo further reaction with the carbonyl electrophile or are stable enough not to undergo further reaction so protonate on work-up. The results are shown in Scheme 5.8.

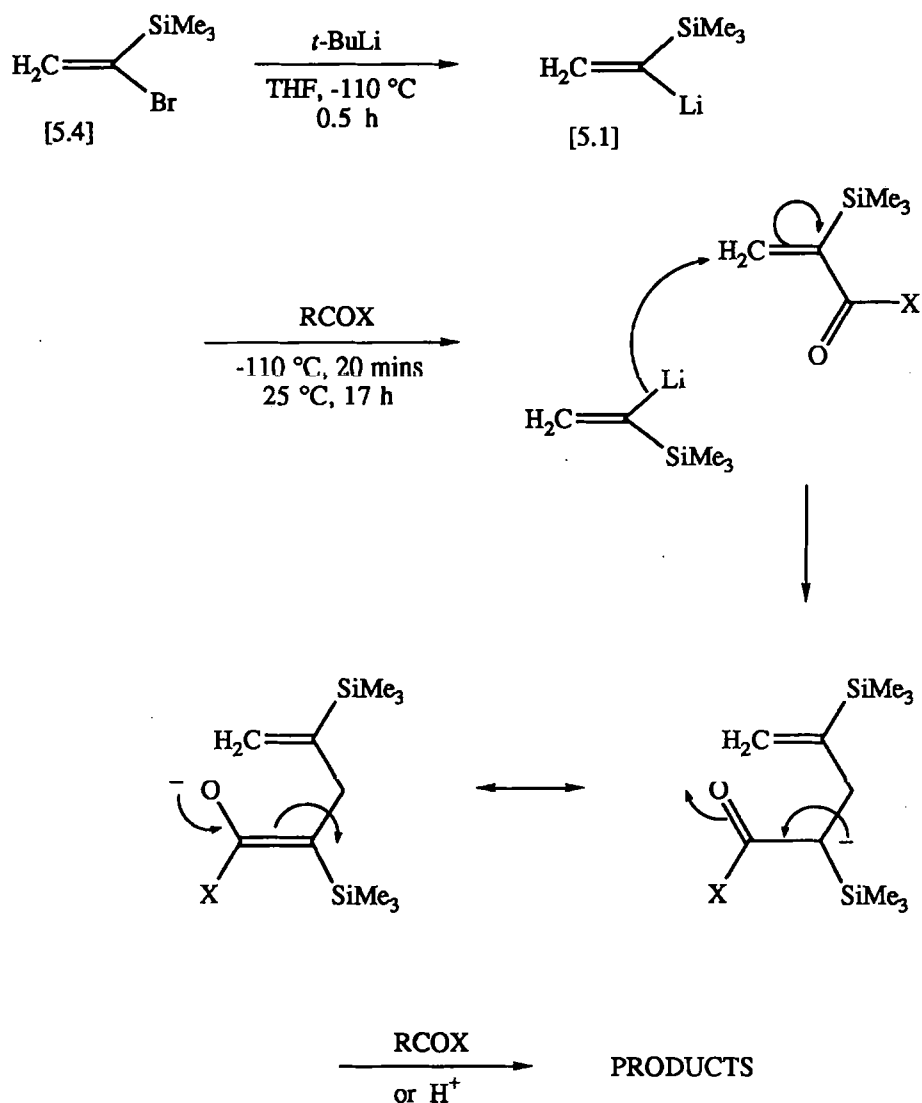
The first reaction attempted was that of  $\alpha$ -lithiovinyltrimethylsilane with ethyl chloroformate. The desired product, ethyl 2-trimethylsilylpropenoate was not obtained as this further reacted by conjugate addition of the  $\alpha$ -lithiosilane. The enolate generated in this way subsequently reacted further with ethyl chloroformate to give the triester compound, 4,4,4-tricarboethoxy-2-trimethylsilylbut-1-ene, [5.21]. The mechanistic aspects of this reaction will be discussed in section 5.5. This prompted us to investigate the reaction of other carbonyl compounds with  $\alpha$ -lithiovinyltrimethylsilane, [5.1]. The carbonyl compounds eventually chosen were ethyl acetate, acetic anhydride, acetyl chloride, phenyl chloroformate and dimethylcarbamyl chloride.

In each case a different course of reaction was followed and the outcome could be explained in terms of the electrophilicity of the carbonyl compound and the reactivity of the intermediate enolate ion. Replacing the  $\alpha$ -lithiovinyltrimethylsilane, [5.1] with the corresponding Grignard reagent in the reaction with ethyl chloroformate yielded the same product. This in itself is not surprising since Grignard reagents in general show a greater tendency towards 1,4-addition than do their lithio counterparts. What is remarkable about these reactions is their high degree of selectivity. Normally reactions of this type lead to a mixture of 1,2- and 1,4-adducts, however in this study the 1,4-adducts are formed exclusively.

#### 5.4.2 Experimental conditions

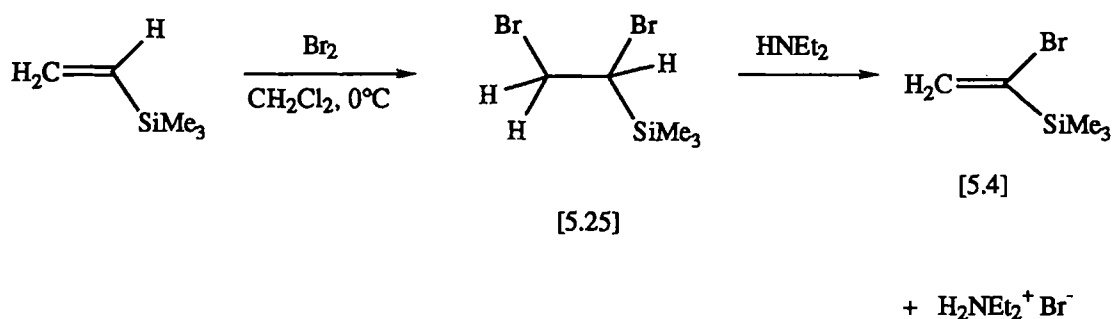
$\alpha$ -Lithiovinyltrimethylsilane, [5.1] was reacted with ethyl chloroformate, ethyl acetate, acetyl chloride, acetic anhydride, phenyl chloroformate and dimethylcarbamyl chloride with

the conditions being the same for each reaction, as described below. The common initial stages of the reaction are outlined in Scheme 5.9.



**Scheme 5.9**

The precursor of the lithiated species is  $\alpha$ -bromovinyltrimethylsilane, [5.4] which is prepared<sup>3</sup> by dehydrobromination of 1,2-dibromoethyltrimethylsilane, [5.25] using diethylamine. The dibromo compound is obtained by addition of bromine to vinyltrimethylsilane (Scheme 5.10).



Scheme 5.10

In a typical run, a THF solution of  $\alpha$ -bromovinyltrimethylsilane [5.4] was cooled with stirring under nitrogen to  $-110^\circ\text{C}$ . *t*-Butyllithium in hexane was then added slowly, carefully maintaining the temperature below  $-100^\circ\text{C}$  throughout, to generate the  $\alpha$ -lithiovinylsilane. *t*-Butyllithium is used in preference to *s*- or *n*-butyllithium in order to suppress coupling of the lithio intermediates with butyl bromide<sup>10</sup>. After a further 30 minutes at this temperature the solution was cooled again to  $-110^\circ\text{C}$  and the electrophile added slowly, dropwise, again maintaining the low temperature. The mixture was then kept for a further 20 minutes at this temperature. After 17 hours at room temperature an aqueous ammonium chloride work-up was followed by purification of the products by column chromatography. The samples were reasonably pure by NMR spectroscopy (>90%) after the work up stage. There was no evidence for any  $\alpha,\beta$ -unsaturated carbonyl compounds which had not undergone a Michael reaction. However, the products were generally contaminated to some extent with *t*-butyl adducts, but these were removed in the early fractions from the column. As with many of the silicon compounds synthesized for this thesis, some decomposition occurred on the silica column, lowering the overall yields of reactions which would otherwise be high yielding.

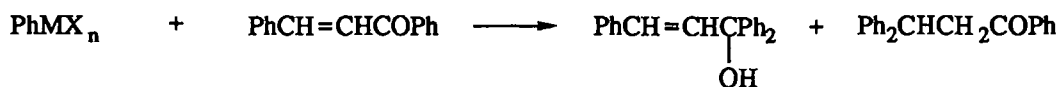
## 5.5 Mechanistic aspects of the reactions of $\alpha$ -lithiovinyltrimethylsilane with carbonyl compounds

### 5.5.1 Overview of the chemistry involved

Common to all of the reactions in the series is the initial attack of the lithio reagent on the electrophile to produce the corresponding  $\alpha,\beta$ -unsaturated carbonyl compound. In no case however, could such an intermediate be isolated. In each case the intermediate  $\alpha,\beta$ -unsaturated carbonyl subsequently reacted with a further molecule of  $\alpha$ -lithiovinyltrimethylsilane in a Michael type addition reaction. With less reactive carbonyl compounds such as ethyl acetate or dimethylcarbonyl chloride, the Michael product protonates to give a stable final product, but with the more reactive electrophiles further reaction was observed.

### 5.5.2 1,2- Versus 1,4-addition

No 1,2-adducts are observed even though reactions of alkylolithium reagents with compounds of the type  $R_2C=CR-COCH_3$  and  $R_2C=CR-COOC_2H_5$  generally lead to 1,2-addition<sup>11</sup>. In reactions of organometallic reagents with  $\alpha,\beta$ -unsaturated carbonyl compounds, there are a number of factors which affect the 1,4-/1,2-addition ratio such as ionic character of the organometallic reagent; reversibility of the 1,2-addition; inductive, resonance and steric effects; choice of solvent; temperature etc. The outcome is normally due to a combination of these factors<sup>12</sup>. In terms of thermodynamics, the formation of the 1,4-addition product should be favoured over that of the 1,2-addition product since the former is stabilized through charge delocalization. In general 1,2-addition is favoured by the more ionic organometallics. This is because the reaction at the carbonyl site represents a 'hard-hard' interaction such that it is kinetically more favourable. This effect is demonstrated by the data<sup>13</sup> shown in table 5.1 (Equation 5.5).

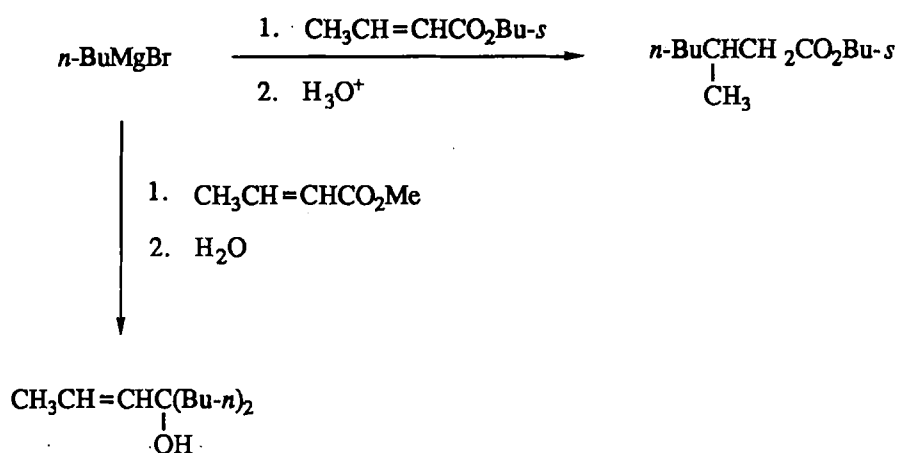


Equation 5.5

Table 5.1

MX <sub>n</sub>	1,2 (%)	1,4 (%)
Na	39	4
Li	69	13
MgBr	0	high
ZnPh	0	91

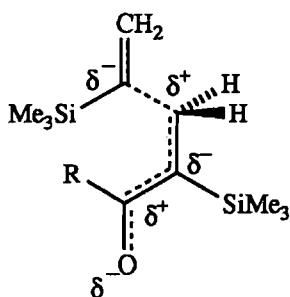
Another important factor is the steric interaction at the carbonyl site. Normally substitution at the carbonyl site in  $\alpha,\beta$ -unsaturated carbonyl compounds has the effect of deflecting nucleophiles towards a 1,4-addition path. An example of this effect is shown in Scheme 5.11<sup>14</sup>.



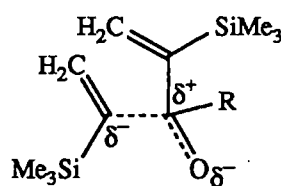
Scheme 5.11

Whereas *n*-BuMgBr undergoes predominantly a 1,4-addition reaction with the *s*-butyl ester of crotonic acid, reaction at the carbonyl site is preferred with less hindered esters. In addition, the fact that  $\alpha,\beta$ -unsaturated aldehydes almost never undergo Michael addition reactions with Grignard or organolithium reagents can at least in part, be attributed to the low steric hindrance at the formyl group.

In this study however the 1,4-addition products are favoured over the 1,2-adducts to the extent that they are formed exclusively. There are a number of explanations as to why such a high level of regioselectivity is observed, but the most convincing concerns the stability of the  $\alpha$ -silyl anion generated in the 1,4-addition reaction. The transition state for this product has lower energy than the transition state for the 1,2-addition product (Figure 5.1). This transition state is stabilized not only by delocalization of charge by conjugation but also, and more importantly, by the effect of the silyl group which stabilizes negative charge build up on the  $\alpha$ -carbon.



transition state for  
1,4-addition



transition state for  
1,2-addition

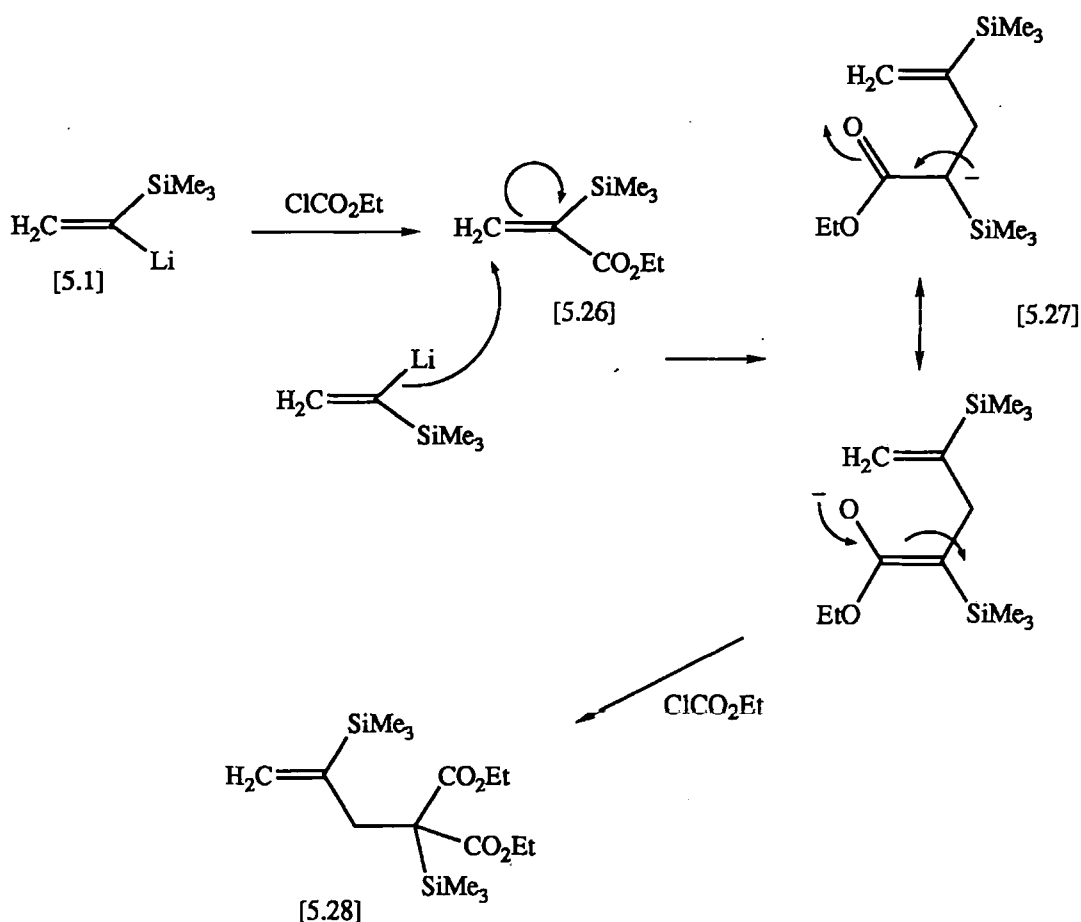
Figure 5.1

Since all of the reactions were carried out under identical conditions, the fate of the intermediate enolate ion is best explained in terms of the nature of the carbonyl compound, in particular its electrophilicity, and the stability of the enolate. There does however,

remain much scope for manipulating the course of the reaction by altering the conditions as will be discussed later.

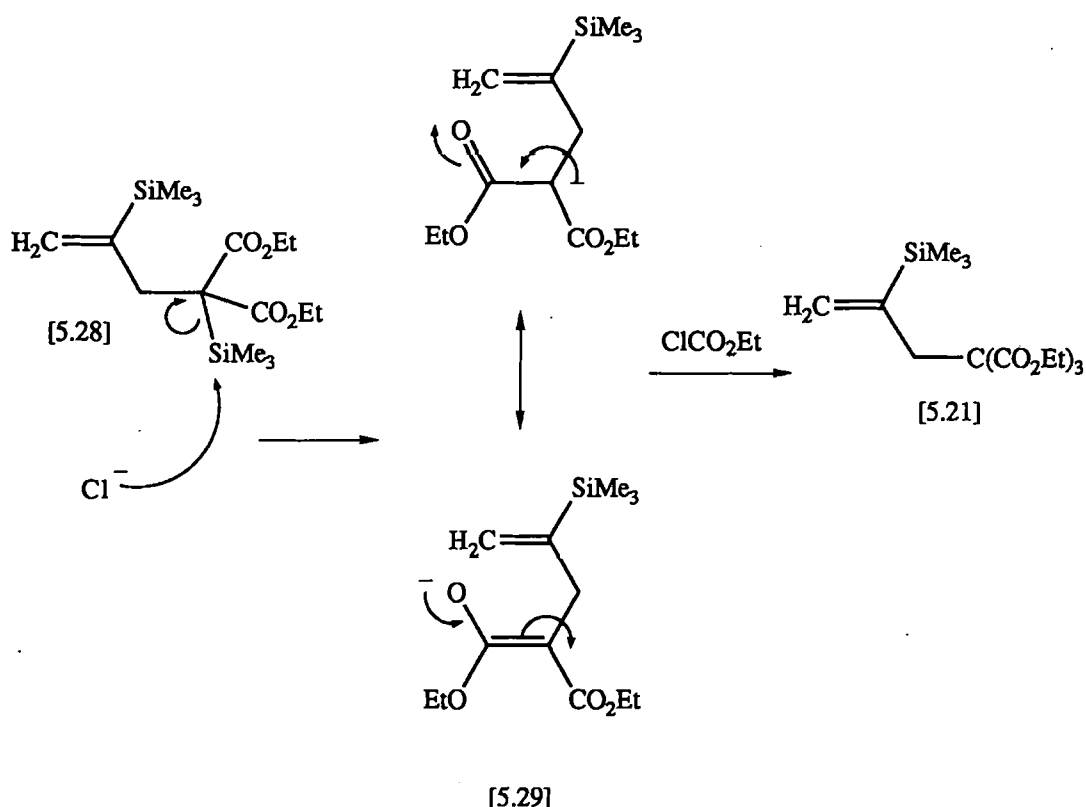
### 5.5.3 The reaction of $\alpha$ -lithiovinyltrimethylsilane with ethyl chloroformate

The first step in this reaction is presumed to be the alkylation of the chloroformate to generate ethyl 2-trimethylsilylpropenoate, [5.26]. The final product however is a triester [5.21] (Scheme 5.12). This can only have been formed by a conjugate addition of  $\alpha$ -lithio vinyltrimethylsilane, [5.1] followed by two more alkylation steps with ethyl chloroformate. It is unlikely that the acrylate intermediate, [5.26] is more reactive than ethyl chloroformate towards addition by [5.1].



Scheme 5.12

However, one would expect the acrylate to be activated towards 1,4-addition reactions through the anion stabilizing properties of the trimethylsilyl group. The most likely explanation for the Michael addition occurring is that the reaction with ethyl chloroformate is fast compared to the rate of addition of the ethyl chloroformate, so that the concentration at any one time of ethyl chloroformate is low compared with that of the propenoate intermediate, [5.26]. The  $\alpha$ -lithiovinyltrimethylsilane, which is in excess under the conditions of the reaction, then reacts somewhat more slowly with the propenoate before more of the chloroformate is added. Once all of the  $\alpha$ -vinyltrimethylsilane is consumed, further addition of ethyl chloroformate results in reaction with the enolate, [5.27] (Scheme 5.12). The diester, [5.29] formed at this stage contains a highly labile carbon-silicon bond. This is because the carbon atom is between two ester groups so an  $S_N2$  displacement reaction would lead to a highly stabilized enolate.



Scheme 5.13

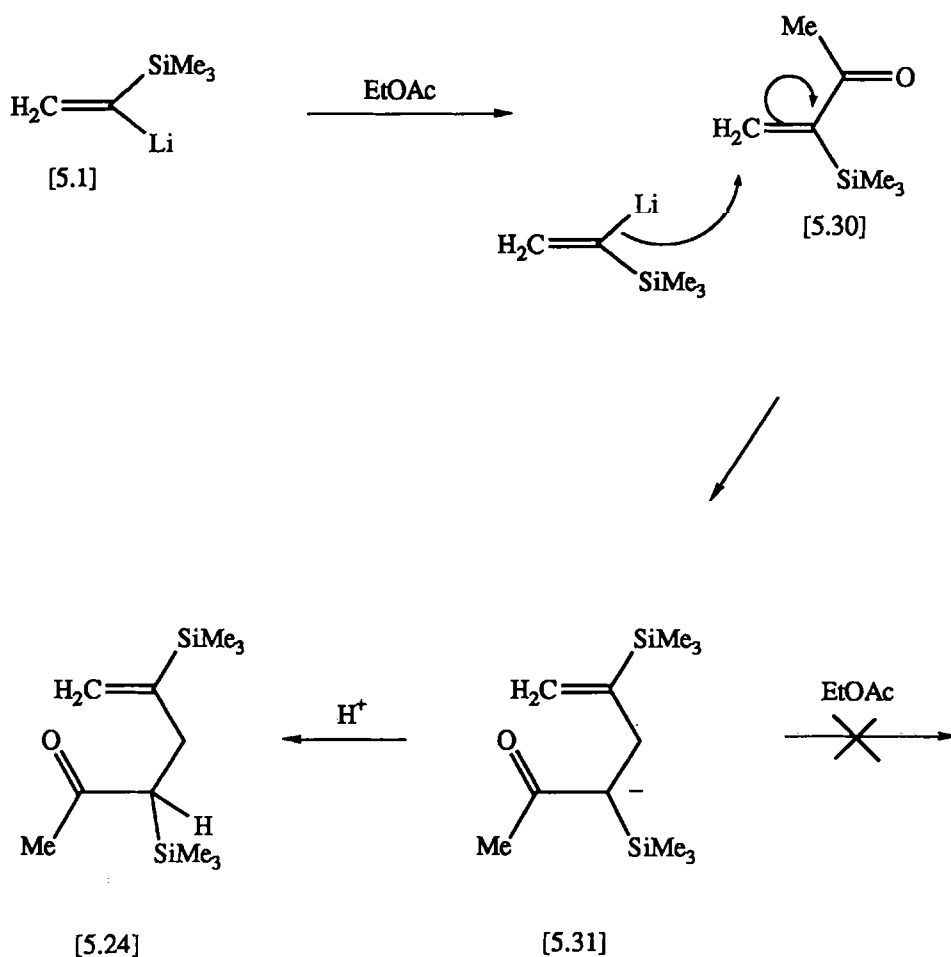


The counterion, chloride, displaced from ethyl chloroformate is a strong enough nucleophile to remove the silyl group. The enolate then reacts with a further molecule of ethyl chloroformate to form the final product (obtained in 92% yield), the triester (Scheme 5.13). The overall stoichiometry of the reaction is 2:3 with respect to  $\alpha$ -lithiovinyltrimethylsilane, [5.1] and ethyl chloroformate. However surprisingly, when a deficiency of ethyl chloroformate is used (i.e., 1:1), the same product, [5.21] is obtained. Obviously in this case, at the end of the reaction, unreacted [5.1] will remain. This implies that the enolate product, [5.27] from the conjugate addition reaction is more reactive towards ethyl chloroformate than is the vinyl anion (although why this should be is not clear). Despite this, no Claisen reaction of the triester with the vinyl lithium compound is observed, probably due to severe steric interactions.

#### 5.5.4 The reaction of ethyl acetate with $\alpha$ -lithiovinyltrimethylsilane

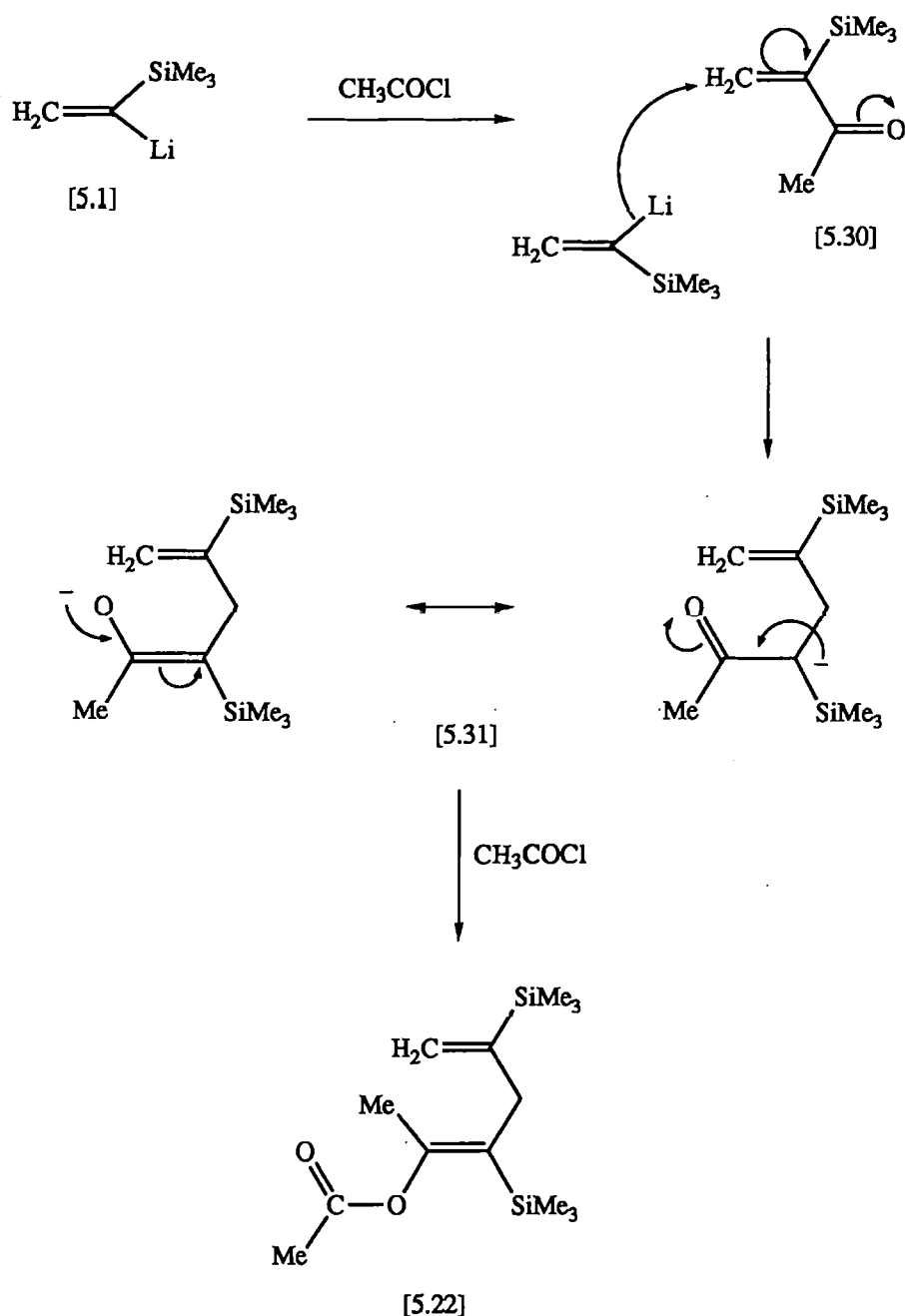
Having successfully produced a triester compound, [5.21] by this route it seemed likely that the method might be a generally applicable one. The possibility of producing a triketone was therefore explored. The electrophile chosen was ethyl acetate. Again there remained the possibility that the vinylketone, [5.30] would be produced as a stable end product. However as in the previously discussed reaction, this underwent a conjugate addition reaction to give a stabilized enolate, [5.31] (Scheme 5.14).

While the ester enolate, [5.29] (Scheme 5.13) at this stage underwent acylation with ethyl chloroformate, no further alkylation was observed with ethyl acetate. This is probably because ethyl acetate is a poor electrophile by comparison, and also the keto enolate, [5.31] is more stable than the ester enolate, [5.29]. The more stable intermediate presumably remains until work-up when protonation occurs. The final product 3,5-bis(trimethylsilyl)hex-5-en-2-one [5.24] is obtained in 48% yield after purification.



**Scheme 5.14**

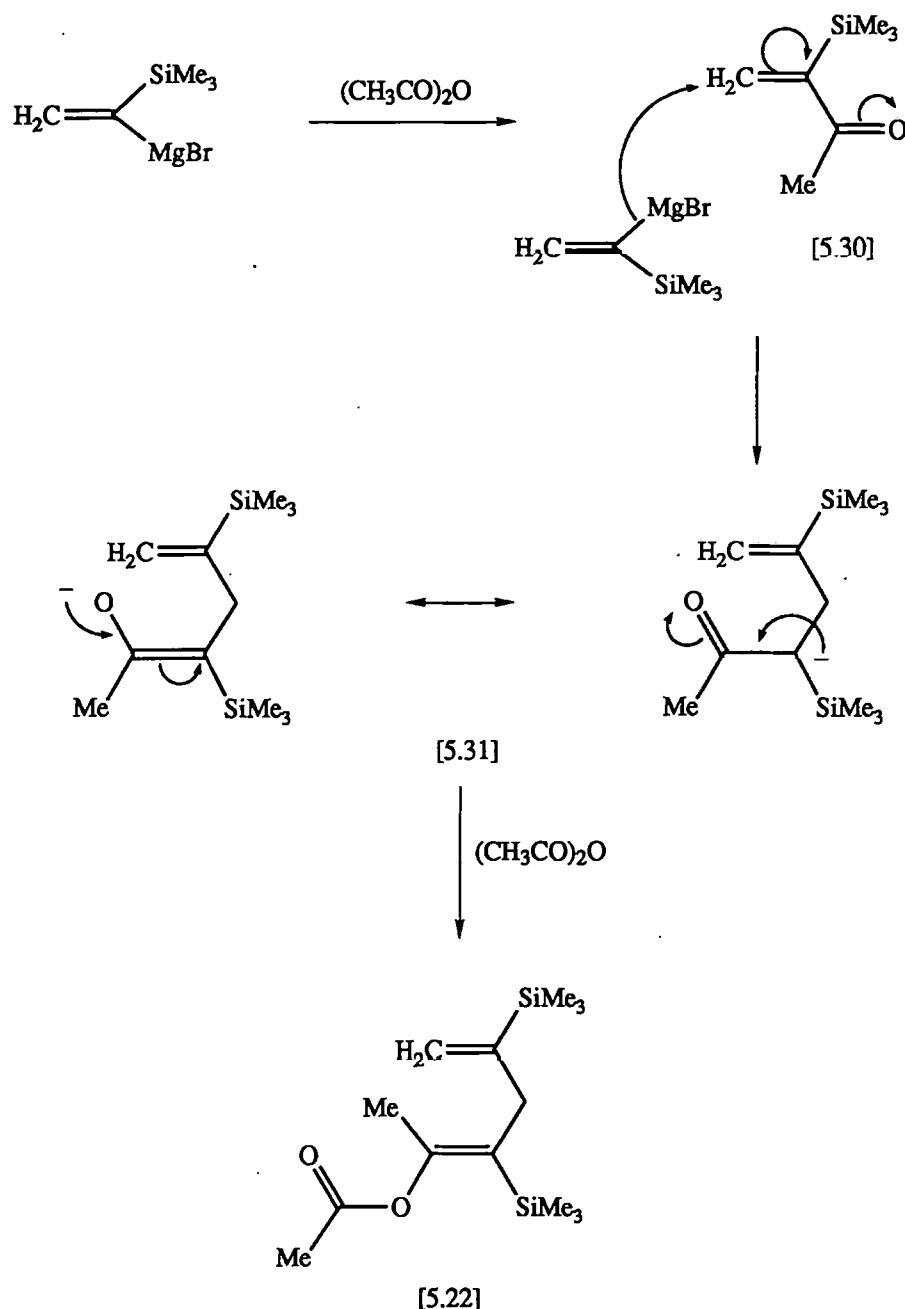
Since ethyl acetate is too poor an electrophile to react with the enolate, [5.31] formed in the previous reaction, it was thought that choosing a more reactive acetylating agent such as acetyl chloride, might lead to further reaction. When the reaction was carried out, further reaction did occur but acetylation did not take place at the carbon site but at the oxygen, thus forming a stable product, 2-acetoxy-3,5-bis(trimethylsilyl)hex-2,5-diene, [5.22] in 21% yield. The mechanism for the formation of this product is shown in Scheme 5.15.



Scheme 5.15

This product, [5.22] could be readily identified as it had already been synthesized by Brook and Duff<sup>7</sup>, by the action of  $\alpha$ -trimethylsilylvinylmagnesium bromide on acetic anhydride in THF-ether (Scheme 5.16). A mixture of the 1:1 adduct (3-trimethylsilylbut-3-en-2-one, [5.30]) and the previously described diene, [5.22] were produced. Temperature is a controlling factor in determining the ratio in which the products are

formed. At  $-120\text{ }^{\circ}\text{C}$  a 1:1 mixture of the compounds is formed whereas a similar experiment carried out at  $-78\text{ }^{\circ}\text{C}$  gave a 1:4 mixture of the  $\alpha,\beta$ -unsaturated ketone [5.30] and diene [5.22] respectively. This would suggest that the Grignard reagent is less active in 1,4-additions to such compounds compared with the corresponding lithio reagent.

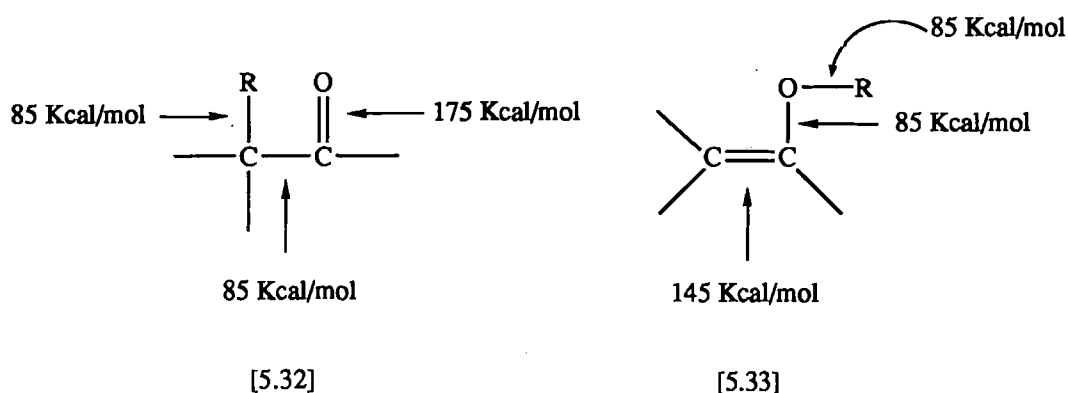


**Scheme 5.16**

### 5.5.5 Carbon versus oxygen alkylation

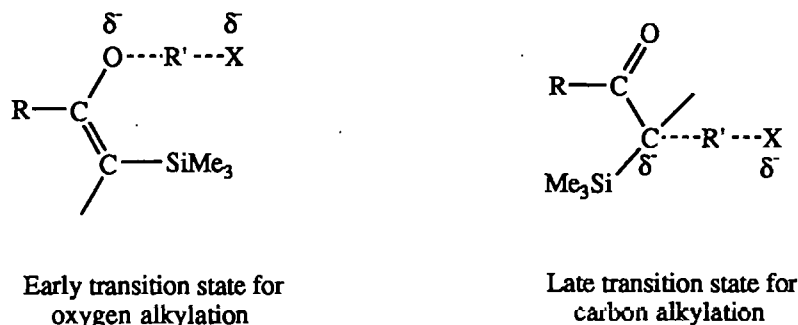
Returning to the present work, there was no evidence for any of the carbon acylation product in the reaction mixture. It is unusual to observe such a high level of regioselectivity<sup>15</sup> in the reactions of enolates with electrophiles. Usually, the use of reactions of this type are hampered by the production of unwanted side products. A mixture of products is normally obtained with a predominance of the carbon alkylation product which is the thermodynamically favoured outcome. Often however it is possible to induce a certain amount of regioselectivity by altering the reaction conditions. The present systems under study may be susceptible to such manipulation although further work is required.

In the absence of any special effects, the carbon alkylated or acylated products of the type [5.32] are thermodynamically more stable than the oxygen analogs [5.33], since the carbonyl bond is stronger than the alkenyl bond as shown below.



If the difference in product stability is strongly reflected in the transition state, the carbon acylation product should predominate. With highly reactive alkylating agents (such as  $\text{ROCH}_2\text{Cl}$ ,  $\alpha$ -haloketones and acid chlorides) the transition state will resemble the reactants with the charge on the enolate moiety concentrated more on the oxygen than carbon - an early transition state. With less reactive alkylating reagents (such as  $\text{RCH}_2\text{Br}$ ) the transition state will resemble more the products - a late transition state. With powerful

electrophiles therefore the transition state for oxygen alkylation has a lower energy than that for carbon alkylation and the product mixture is subject to kinetic control. The charge distribution in the two transition states can be seen in Figure 5.2.



**Figure 5.2**

The actual carbon/oxygen alkylation ratios observed can be a function of a number of factors. Factors which contribute to the oxygen site being more 'naked' have the effect of promoting oxygen alkylation. Since the concentration of negative charge in an enolate species is greater on oxygen than on carbon there is a greater tendency for ion pairing or solvation by hydrogen bonding to occur at the oxygen site. As a result the more coordinated oxygen atom is less available as a nucleophile and the carbon atom may become the more nucleophilic site.

Solvents have a dominant role in determining regioselectivity. Protic solvents have the effect of promoting carbon alkylation since they have a greater tendency to solvate (by hydrogen bonding) the more electronegative oxygen site. However polar aprotic solvents such as DMF or DMSO are more effective in solvating cations, leaving the oxygen anion 'naked', thereby increasing the ratio of oxygen attack. Crown ethers have the same effect.

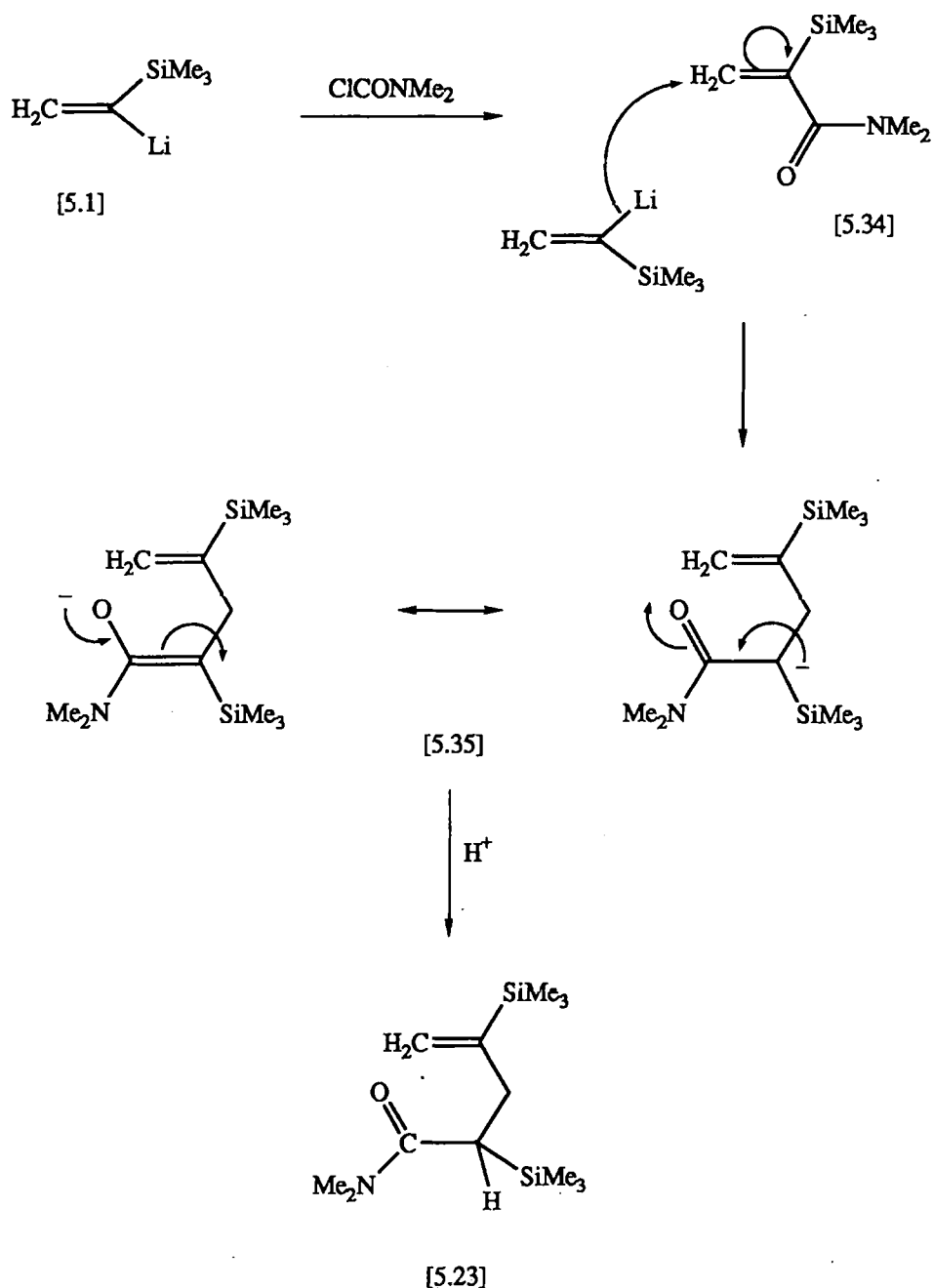
The nature of the counter ion also has an effect. 'Softer' cations such as  $\text{Mg}^{2+}$  tend to form a less tight ion pair with the oxygen than do 'harder' ones such as  $\text{Li}^+$ . Likewise the softness of the alkylating agent tends to follow a trend such that the carbon/oxygen ratio increases in the series  $\text{ROT} < \text{RCl} < \text{RBr} < \text{RI}$ .

#### 5.5.6 Reaction of $\alpha$ -lithiovinyltrimethylsilane with acetic anhydride

Acetic anhydride is a somewhat milder acylating agent than acetyl chloride. However it is still a good electrophile and leads to the same oxygen acylated product, 2-acetoxy-3,5-bis(trimethylsilyl)hex-2,5-diene, as was obtained in the acetyl chloride reaction. Compared to that of acetyl chloride however the product mixture was much cleaner and almost quantitative yields of product were obtained (yield after purification, 84% compared with 21% for the acetyl chloride reaction).

#### 5.5.7 Reaction of $\alpha$ -lithiovinyltrimethylsilane with dimethylcarbonyl chloride

The reaction of  $\alpha$ -lithiovinyltrimethylsilane with dimethylcarbonyl chloride follows the same course of reaction as that by ethyl acetate and is depicted in Scheme 5.17. In common with ethyl acetate, dimethylcarbonyl chloride is a relatively weak electrophile. Consequently it does not react readily with the enolate, [5.35] which eventually protonates on work-up to give [5.23]. The reaction is less clean however and lower yielding. The product decomposed extensively on silica and so the overall yield was only 7%, although this is not a reflection of the efficiency of the reaction.



**Scheme 5.17**

#### 5.5.8 Reaction of $\alpha$ -lithiovinyltrimethylsilane with phenyl chloroformate

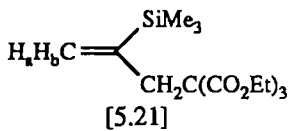
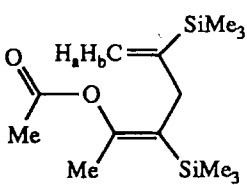
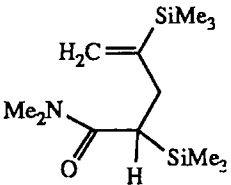
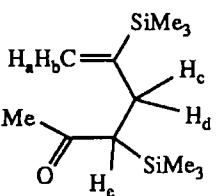
When the reaction was carried out using phenyl chloroformate, a black oily product was obtained. This was observed to be a mixture of several compounds and no attempts were made to purify the mixture. The reaction was not repeated.



## 5.6 Spectroscopic Features

All of the products could be readily identified by NMR spectroscopy. In the case of [5.22] this had already been prepared by Brook and Duff<sup>7</sup>.

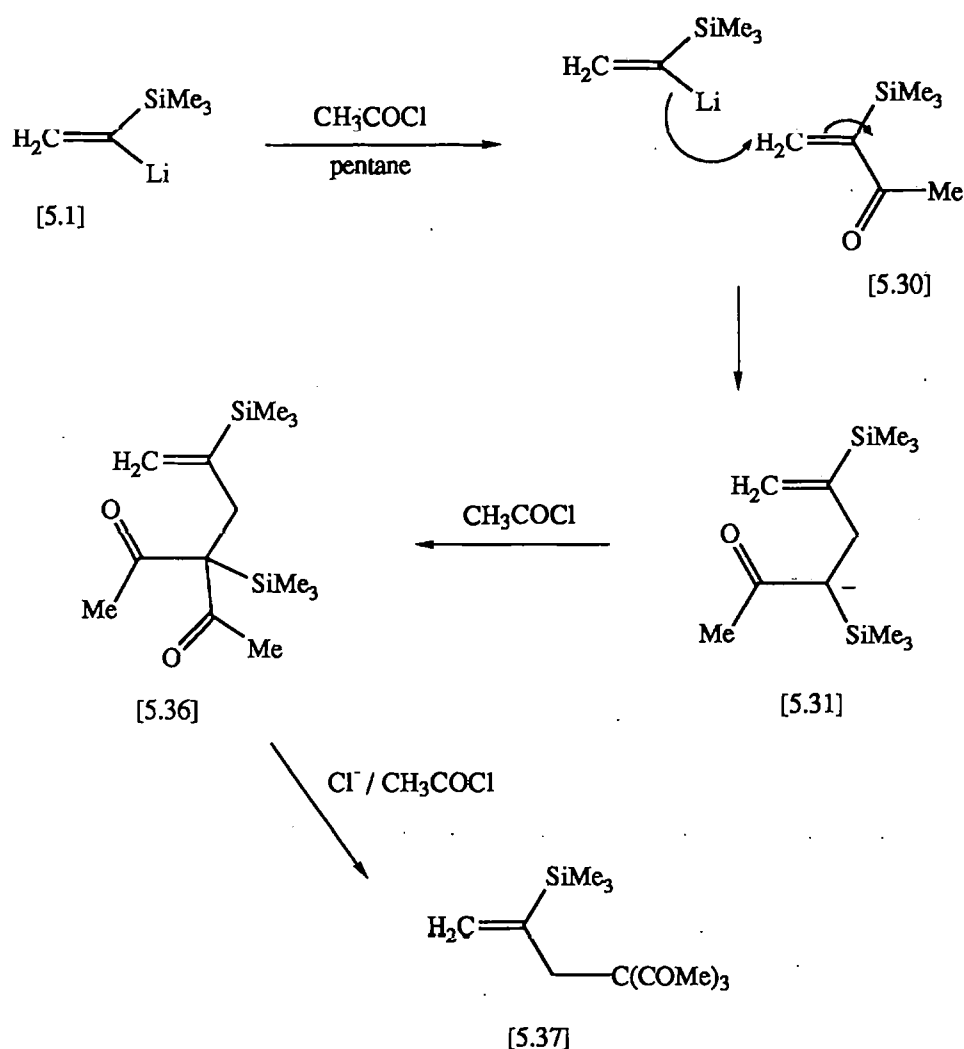
Table 5.2 NMR Spectroscopic Data<sup>1</sup>

Entry	NMR Data
 <p>[5.21]</p>	<p><sup>1</sup>H 0.15 (9 H, s, Me<sub>3</sub>Si), 1.29 (9 H, q, 3 x CH<sub>2</sub>CH<sub>3</sub>), 3.02 (2 H, s, CH<sub>2</sub>C(CO<sub>2</sub>Et)), 4.25 (6 H, t, 3 x CH<sub>2</sub>CH<sub>3</sub>), 5.48 (1 H, s, H<sub>a</sub>), 5.69 (1 H, s, H<sub>b</sub>). The geminal coupling constant between H<sub>a</sub> and H<sub>b</sub> is observed to be zero.</p> <p><sup>13</sup>C 0.80 (Me<sub>3</sub>Si), 14.8 (CH<sub>3</sub>), 37.6 (CH<sub>2</sub>CSi), 62.8 (CH<sub>2</sub>O), 66.5 (C(CO<sub>2</sub>Et)<sub>3</sub>), 127.3 (H<sub>2</sub>C=), 147.0 (CSiMe<sub>3</sub>), 167.5 (C=O).</p> <p><sup>x</sup>Si -52.73.</p>
 <p>[5.22]</p>	<p><sup>1</sup>H 0.03 and 0.08 (2 x 9 H, s, 2 x Me<sub>3</sub>Si), 1.96 (3 H, s, MeC=C), 2.08 (3 H, s, MeCO), 2.74 (2 H, s, CH<sub>2</sub>), 5.22 (1 H, d, J 2.4 Hz, H<sub>a</sub>), 5.38 (1 H, m, H<sub>b</sub>).</p> <p><sup>13</sup>C -3.6 and -3.3 (2 x Me<sub>3</sub>Si), 20.0 (MeC=C), 20.8 (MeC=O), 33.8 (CH<sub>2</sub>), 120.3 (MeC=C), 123.3 (H<sub>2</sub>C=), 149.2 (MeC=C), 151.7 (H<sub>2</sub>C=C), 168.7 (C=O).</p>
 <p>[5.23]</p>	<p><sup>13</sup>C -1.76 and -0.83 (2 x Me<sub>3</sub>Si), 32.20 (CH<sub>3</sub>), 32.8 (CH<sub>2</sub>CHCO), 48.3 (CHCO), 124.2 (H<sub>2</sub>C=), 152.1 (SiC=), 209.9 (C=O).</p>
 <p>[5.24]</p>	<p><sup>1</sup>H [0.10 (3 H, s); and 0.11 (3 H, s) Me<sub>3</sub>Si's], 2.04 (3 H, s, CH<sub>3</sub>), 2.19 (1 H, dd, CH<sub>c</sub>H<sub>d</sub>), 2.67-2.75 (2 H, m, CH<sub>c</sub>H<sub>d</sub> and CH<sub>e</sub>), 5.27 (1 H, s, CH<sub>a</sub>H<sub>b</sub>), 5.47 (1 H, s, H<sub>a</sub>H<sub>b</sub>C=). The geminal coupling constant between H<sub>a</sub> and H<sub>b</sub> is observed to be zero.</p> <p><sup>13</sup>C -2.5 and -1.5 (Me<sub>3</sub>Si's), 31.6 (CH<sub>3</sub>), 32.6 (CH<sub>c</sub>H<sub>d</sub>), 47.6 (CH<sub>e</sub>), 123.7 (CH<sub>a</sub>H<sub>b</sub>), 151.4 (SiC=), 209.3 (C=O).</p>

<sup>1</sup>All of the spectra were recorded on a 400 MHz instrument.

## 5.7 Conclusions

The action of  $\alpha$ -lithiovinyltrimethylsilane on activated carbonyl compounds represents a highly versatile new route to highly functionalized vinylsilanes. The success of the reactions studied points towards further work including; manipulation of regiochemistry of addition of electrophiles; use of new electrophiles; and attempts to suppress the Michael reaction in order to isolate the silylenones.



Scheme 5.18

There are a number of experiments that can be carried out in order to test regioselective control. With acetyl chloride and acetic anhydride the second alkylation step occurs at the

oxygen site. It may be possible to alter the course of reaction in favour of carbon alkylation by choosing a non-polar solvent such as pentane (Scheme 5.18). Such solvents are ineffective in solvating the counter cation causing greater ion-pairing at the oxygen, making carbon the more nucleophilic site. Thus, under these conditions, the enolate [5.31] might be made to react further to give [5.36] or [5.37] as end products. All of the other reactions underwent carbon acylation. These may be susceptible to regioselective manipulation by the use of polar aprotic solvents and crown ethers which will solvate the cations. Also, changing to a softer cation such as  $Mg^{2+}$  may promote oxygen alkylation as these form a less tight ion pair with the hard oxygen anion. This might be achieved by using a Grignard rather than a lithio reagent. Although one reaction carried out by the Grignard route (with ethyl chloroformate as the alkylating agent) gave the same product as obtained by the lithio route, the reaction is still worth investigating with new solvents.

When ethyl acetate and dimethylcarbamy chloride were used as electrophiles in the reaction only one alkylation step took place indicating that these are too poorly electrophilic to react with the Michael enolates. It may therefore be possible to perform a mixed reaction by adding a stronger electrophile at this point as in Equation 5.6.



Equation 5.6

## 5.8 References

1. E.D. Bergmann, D. Ginsburg and R. Pappo, *Org. React.*, **10**, 179, (1959).
2. W.S. Rapson and R. Robinson, *J. Chem. Soc.*, 1285, (1935).
3. A. Ottolenghi, M. Fridkin, and A. Zilkha, *Can. J. Chem.*, **41**, 2977, (1963).
4. E. Lukevics and V. Direns in "Frontiers of Organosilicon Chemistry", Ed. A.R. Bassindale and P.P. Gaspar, The Royal Society of Chemistry, Cambridge, 1991, p. 383.
5. G. Stork and B. Ganem, *J. Am. Chem. Soc.*, **95**, 6152, (1973).
6. A.R. Bassindale and P.G. Taylor in "The Chemistry of Organic Silicon Compounds", Ed. S. Patai and Z. Rappaport, John Wiley and Sons, (1989) p. 893.
7. A.G. Brook and J.M. Duff, *Can. J. Chem.*, **51**, 2024, (1973).
8. O. Tsuge, S. Kanemasa, and Y. Ninomiya, *Chem. Lett*, 1993, (1984).
9. J. Tanaka, S. Kanemasa, H. Kobayashi, and O. Tsuge, *Chem. Lett.*, 1453, (1989).
10. G. Zweifel and W. Lewis, *J. Org. Chem.*, **43**, 14, 2739 (1978).
11. Rozhkov and Makin, *J. Gen. Chem, USSR*, **34**, 57 (1964).
12. E.I. Negishi, "Organometallics in Organic Synthesis, Vol. 1", Wiley (Interscience), New York, 1980, p. 127.
13. H. Gilman, and R.H. Kirby, *J. Am. Chem. Soc.*, **63**, 2046, (1941).
14. J. Munch-Peterson, *J. Org. Synth.*, **41**, 60, (1961).
15. E.I. Negishi, "Organometallics in Organic Synthesis, Vol. 1", Wiley (Interscience), New York, 1980, p. 186.

## CHAPTER 6

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### EXPERIMENTAL

#### Measurement of data

##### NMR Spectra

NMR spectra were recorded as solutions in deuterated chloroform with tetramethylsilane as an internal standard using (unless stated otherwise), a Jeol FX90 Q multinuclear spectrometer. In certain other cases stated in the text a Bruker JNM-EX400 was used to record the spectra. The 400 MHz instrument was only available when the latter part of the research was conducted so NMR analysis of the products obtained during the earlier stages of the work could only be carried out using a 90 MHz instrument. In certain cases however, stable samples were later analysed on the higher resolution instrument.

##### IR Spectra

IR spectra were recorded on a Nicolet 205 FT IR spectrometer.

##### Mass Spectra

Mass spectra were recorded on a VG20-250 mass spectrometer. Exact mass analyses were carried out by Hoescht, however spectra showing the breakdown were not provided.

##### Elemental Analysis

Elemental analyses were carried out by Medac Ltd. Although the samples submitted for analysis were known to be pure by other methods, the carbon content found was frequently lower than that required. This may be due to the formation of silicon carbides during the combustion process.

##### U.V. Irradiation

Photolysis reactions were carried out using a medium pressure arc carousel (rayonet) at 254 nm.

### Thin-layer and column chromatography

Thin-layer chromatography was carried out using silica gel UV<sub>254</sub> (0.25 mm) plates. Compounds were visualized using u.v. light. Column chromatography was carried out using silica-gel, 60Å, obtained from Rhone-Poulenc.

### Handling of moisture sensitive compounds

Many of the reactions carried out required anhydrous conditions. In such cases the reactions were carried out under a slow stream of nitrogen. The moisture sensitive reagents were stored under nitrogen in teflon sealed glass vials. Where appropriate, the reagents were measured by volume and introduced to the reaction vessel using a gas tight syringe, via a *suba seal* stopper. When possible, the reactions were carried out entirely within a nitrogen flushed glove box.

### Sources and Purification of reagents

#### 1. Solvents

*Diethylether* was obtained from BDH Ltd and dried by distillation from sodium wire.

*Tetrahydrofuran* was obtained from BDH Ltd and dried by refluxing over, and distillation from calcium hydride using benzophenone as a moisture indicator.

*Hexane*, obtained from Rathburns Ltd was glass distilled grade and not further purified prior to use.

*Acetonitrile*, *carbon tetrachloride* and *acetone* were 'Analar' reagents from BDH Ltd and stored over 4Å molecular sieves and under nitrogen.

*Ethanol (absolute)* was obtained from Hayman Ltd and was not further purified prior to use.

*Ethyl acetate* and *methanol* were obtained from BDH Ltd and distilled prior to use.

Pentane and 1,4-dioxane were obtained from Aldrich Chemical Co. and not further purified prior to use.

*Dichloromethane* was obtained from BDH Ltd and distilled from calcium chloride prior to use.

## 2. Starting materials

The following materials were used without purification:

Ammonium chloride, ammonium hydroxide, calcium hydride, magnesium turnings, magnesium sulphate, sodium bicarbonate, potassium fluoride, cesium fluoride, bromine, ammonia, trifluoroacetic acid, acetic anhydride, acetic acid, (BDH Ltd).

Phenylhydrazine hydrochloride, ethyl chloroformate, methyl chloroformate, 1*M* hydrogen chloride solution in ether, methyl iodide, phenyl chloroformate, acetyl chloride, dimethylcarbonyl chloride, triphenylphosphine, methyl propynoate, dimethylphenylsilane, diphenylmethylsilane, palladium on activated carbon (0.5%, 5%, and 10%), Lindlar catalyst, platinum on activated carbon, *N*-bromosuccinimide, perchloric acid, sodium hydride, sodium azide, (Aldrich Chemical Co.).

Gaseous hydrogen chloride and hydrogen bromide (Fisons Scientific Apparatus).

Vinyltrimethylsilane and vinyltriphenylsilane (Lancaster Synthesis).

Divinyldimethylsilane (Dow Corning).

The following reagents were stored under nitrogen:

Boron trifluoride etherate, trimethylsilyl chloride, trimethylsilyl bromide, trimethylsilyl iodide, trifluoromethanesulphonic acid, methyl trifluoromethanesulphonic acid, trimethylsilyl trifluoromethanesulphonic acid, K-selectride, tetrabutylammonium fluoride supported on silica gel, tetrabutylammonium fluoride 1.0*M* solution in THF, tetrabutylammonium fluoride trihydrate, tetraphenylphosphonium bromide, 18-crown-6, (Aldrich Chemical Co.).

The following reagents were stored in a desiccator:

Calcium hydride and lithium aluminium hydride.

Butyllithium solutions were obtained from Aldrich Chemical Co. and stored at room temperature under nitrogen. They were regularly standardized according to the method of Gilman<sup>1</sup>.

The following reagents were obtained from Aldrich Chemical Co., and purified prior to use:

*Diethylamine, benzylamine and aniline* were dried by refluxing over and distilling from potassium hydroxide.

*Pivaldehyde, propionaldehyde and hexanal* were purified by fractional distillation.

*Benzaldehyde* was washed with sodium carbonate and sodium sulphite solutions then dried with calcium chloride and fractionally distilled.

*Acetaldehyde* was washed with sodium bicarbonate solution, dried with calcium hydride and fractionally distilled.

*Acetyl chloride* was dried by refluxing over phosphorous pentoxide then distilled.

*Acetic anhydride* was purified by refluxing over calcium hydride followed by fractional distillation.

*Acetone* was dried using 4Å molecular sieves then distilled.

*Cuprous iodide* was dried by the following method. Cuprous iodide (6.57 g) was dissolved in an aqueous (50 ml) solution of KI (65.0 g) and 0.25 g activated charcoal was added. The brown mixture was stirred for 10 minutes and then filtered to give a colourless solution which was diluted with distilled water causing a white solid to precipitate. This was washed with distilled water, acetone and ether then dried *in vacuo* overnight. The material was then further dried by soxhlet extraction (24 hours) in THF.

*Diethylmalonate* was dried with calcium chloride and then distilled.

*Cyclohexanone* was dried with sodium sulphate and then distilled.

## Synthesis of starting materials

### Alkyl azidoformates

Ethyl azidoformate and methylazidoformate were prepared according to the method of Forster and Fierz<sup>2</sup>.



## Vinylsilanes

*Trans*-trimethylsilylstyrene and *trans*-trimethylsilylhex-1-ene were prepared according to the method of Benkeser and Hickner<sup>3</sup>. Methyl 2-(triethylsilyl)propenoate was prepared by the method of Lukevics<sup>4</sup>.  $\alpha$ -Bromovinyltrimethylsilane was prepared according to the method of Ottolenghi<sup>5</sup>.

### 1-Phenyl-2-trimethylsilylaziridine

1-Phenyl-2-trimethylsilylaziridine was prepared according to the method of Soobramanien<sup>6</sup>.

### Cis-3-phenyl-1-propyl-2-trimethylsilylaziridine

*Cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine was prepared according to the method of Soobramanien<sup>6</sup>.

## Phenyl Azide

Phenyl azide was prepared according to the method of Lindsay and Allen<sup>7</sup>.

### Note on compound identification in this Chapter

Since individual compounds will have different numbers if they arise in more than one Chapter, any number associated with a compound refers back to the Chapter wherein the process described is introduced.

## 6.1 Preparation of silylbromoazides from vinylsilanes (method A)

With the modifications given below, the following general method, which is similar to that used by Duboudin<sup>8</sup>, was applied to the synthesis of bromoazides from *trans*-trimethylsilylstyrene, triphenylvinylsilane, and divinyl dimethylsilane. The method is described for *trans*-trimethylsilylstyrene. The regiochemical assignments for the products can be confirmed by comparison with similar known structures and/or can be predicted from consideration of the mechanism. This is discussed in full in Chapter 2 for all of the structures.

### (i) RS/SR-2-azido-1-bromo-2-phenyl-1-trimethylsilylethane. [2.18]

Bromine (8.00 g, 50 mmol) was added dropwise to an ice-cooled mixture of sodium azide (32.5 g, 500 mmol) in 100 ml of dichloromethane containing 25 ml of 30% hydrochloric acid. The mixture was stirred for 45 minutes at 45 °C. The organic layer containing the bromine azide was decanted from the aqueous layer and suspended solids, and added dropwise to a stirring, pre-cooled (-5 °C) solution of *trans*-trimethylsilylstyrene (8.80 g, 50 mmol) in dichloromethane. The mixture was stirred for 45 minutes at 0 °C. Washing with two 50 ml portions of dilute sodium bicarbonate solution was followed by rotary evaporation at room temperature to give RS/SR-2-azido-1-bromo-2-phenyl-1-trimethylsilylethane as a pale pink oil, (12.5 g, 42 mmol, 84%). This was contaminated by a small amount (*ca* 5% by NMR spectroscopy) of the SS/RR adduct. Chromatography failed to separate the diastereoisomers and so the product was used as a mixture. Since the product was unstable, elemental analysis was not possible.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 0.09 (9 H, s, Me<sub>3</sub>Si), 3.68 (1 H, d, *J* 9.03 Hz, CHBr), 4.84 (1 H, d, *J* 9.03 Hz, CHN<sub>3</sub>), 7.42 (5 H, s, Ph).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) -1.6 (Me<sub>3</sub>Si), 47.4 (CSi), 69.9 (CN<sub>3</sub>), 127.9, 129.5, 129.7 and 129.4 (Ph).  $\nu_{\text{max}}$ . 2100 (str.), 1490, 1450, 1430, 1310, 1240, 740 and 700 cm<sup>-1</sup>.

(ii) 2-Azido-1-bromo-1-triphenylsilylethane

In a modification to the general procedure, this azide was made using an increased proportion of sodium azide to bromine, in order to preclude formation of the dibromo adduct. Also, the product mixture was stirred at room temperature for an additional 7 hours prior to work-up to ensure complete reaction. The reaction was carried out using: bromine (4.8 g, 30 mmol); sodium azide (30.0 g, 462 mmol) and 20% hydrochloric acid (21 ml). Evaporation of the organic layer yielded a pale orange solid. This crystallized from a mixture of chloroform and hexane in the ratio 2:5, to give 2-azido-1-bromo-1-triphenylsilylethane as a white solid, (6.85 g, 16.8 mol, 56%).  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 3.36 (1 H, dd,  $J$  10.4 and 13.6 Hz, HCB $\text{r}$ ), 3.89 (1 H, dd,  $J$  2.8 and 13.6 Hz,  $\text{H}_a\text{H}_b\text{CN}_3$ ), 4.10 (1 H, dd,  $J$  2.8 and 10.4 Hz,  $\text{H}_a\text{H}_b\text{CN}_3$ ), 7.46-7.69 and 7.75-7.95 (15 H, m, Ph).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) 37.0 (CSi), 54.8 ( $\text{CN}_3$ ), 127.6, 130.1, 131.2 and 135.8 ( $\text{Ph}_3$ ).

(iii) Bis (2-azido-1-bromoethyl)dimethylsilane

This was prepared by the general method described above using: divinyl dimethylsilane (5.0 g, 44.6 mmol); bromine (21.4 g, 134 mmol); sodium azide (87 g, 1.34 mol); 30% HCl (67 ml) and 250 ml dichloromethane. Yield 12.5 g, 35.1 mmol, 79%.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.26 and 0.38 (2 x 3 H, 2 x s, SiMe $_a$  and SiMe $_b$ ), 3.22-3.98 (6 H, m, 2 x CHCH $_2$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -5.8 and -5.2 (SiMe $_a$ Me $_b$  and SiMe $_a$ Me $_b$ ), 39.2 (CBr), 54.0 ( $\text{CN}_3$ ).  $\nu_{\text{max}}$ . 2100 (str.), 1720 (br.), 1260, 840 and 800  $\text{cm}^{-1}$ . The two methyl groups on the silicon are diastereotopic correspondingly, two resonances are observed in both the  $^{13}\text{C}$  and  $^1\text{H}$  NMR spectra.

## 6.2. Preparation of silylbromoazides from vinylsilanes (method B)

This method was used to prepare the corresponding bromoazides from *trans*-trimethylsilylstyrene and *trans*-1-trimethylsilylhex-1-ene. The method is described for *trans*-trimethylsilylstyrene.

(i) SS/RR-2-azido-1-bromo-2-phenyl-1-trimethylsilylethane, [2.17]

*N*-Bromosuccinimide (24.0 g, 135 mmol) was added in small portions to a pre-cooled (-6 °C) stirred mixture of aqueous (100 ml) sodium azide (22.3 g, 343 mmol) in 1,4-dioxane (300 ml) containing the alkene, *trans*-trimethylsilylstyrene (16.9 g, 96.2 mmol). The mixture was then stirred at 0 °C until the orange colour of the bromine azide disappeared, (30 minutes - 1 hour) and a clear solution remained. This was washed several times with brine and extracted with ether. Following concentration, residual succinic acid was removed by precipitation in carbon tetrachloride. The product oil, SS/RR-2-azido-1-bromo-2-phenyl-1-trimethylsilylethane was recovered as a single diastereoisomer and purified by flash column chromatography on silica using neat hexane as the eluent. Yield, 20.6 g, (69.1 mmol, 72%).  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 0.24 (9 H, s, Me<sub>3</sub>Si), 3.64 (1 H, d, *J* 8.4 Hz, CHBr), 4.84 (1 H, d, *J* 8.4 Hz, CHN<sub>3</sub>), 7.32 (5 H, s, Ph).

(ii) 2-Azido-1-bromo-1-trimethylsilylhexane, [2.22]

This was prepared in 71% yield, as a colourless oil, by the general method using: *N*-bromosuccinimide (24.0 g, 135 mmol); sodium azide (22.3 g, 343 mmol) and *trans*-1-trimethylsilylhex-1-ene (15.0 g, 96.2 mmol).  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 0.21 (9 H, s, Me<sub>3</sub>Si), 0.80-1.05 (3 H, m, CH<sub>3</sub>), 1.10-2.80 (6 H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 3.39 (1 H, d, *J* 5.1 Hz, CHBr), 3.49-3.95 (1 H, m, CHN<sub>3</sub>).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) 0.6 (Me<sub>3</sub>Si), 14.1 (CH<sub>3</sub>), 24.6 (CH<sub>2</sub> CH<sub>3</sub>), 30.8 (CH<sub>2</sub>CH<sub>2</sub> CH<sub>3</sub>), 35.4 (CH<sub>2</sub>CHN), 47.8 (CSi), 67.7 (CN). C<sub>9</sub>H<sub>20</sub>N<sub>3</sub>BrSi requires: C, 38.84; H, 7.24%. Found C, 38.96; H, 7.52%.  $\nu_{\text{max}}$ . 2960, 2100 (str.), 1250 and 840 cm<sup>-1</sup>.

### 6.3 Procedure for the lithium aluminium hydride reduction of silylbromoazides to the corresponding silylaziridines

This method was applied in the synthesis of: *cis*-3-phenyl-2-trimethylsilylaziridine; *trans*-3-phenyl-2-trimethylsilylaziridine and 2-triphenylsilylaziridine. The method is described for the reduction of RS/SR-2-azido-1-bromo-2-phenyl-1-trimethylsilylhexane. In the case of bis(2-azido-1-bromoethyl)silane (6.3 (iii)), the major product obtained was dimethyl di(2-aminoethyl)silane. With 2-azido-1-bromo-1-trimethylsilylhexane, 2-amino-1-trimethylsilylhexane was obtained and this reaction is described in section 6.4 (i).

#### (i) *Cis*-3-phenyl-2-trimethylsilylaziridine. [2.20]

A slurry of lithium aluminium hydride (1.7 g, 44.8 mmol) in dry ether (30 ml) was cooled (ice-salt bath) with stirring under nitrogen. RS/SR-2-azido-1-bromo-2-phenyl-1-trimethylsilylhexane (95%, 4.6 g, 14.7 mmol) in dry ether (5 ml) was added dropwise during 10 minutes, carefully maintaining the temperature below 0 °C. Slight effervescence was accompanied by the production of a pale olive green colour. The mixture was stirred for a further 45 minutes at 0 °C and then allowed to warm to room temperature. Stirring was continued for a further 17 hours. Re-cooling to 0 °C was followed by slow hydrolysis with 9 ml of a 20% sodium hydroxide solution, added dropwise with stirring over a period of 15 minutes. After warming to room temperature the mixture was stirred rapidly for 45 minutes. The resultant fine white granular solid was washed well with ether and the mother liquor and washings were carefully dried with magnesium sulphate over several hours. Concentration gave 2.6 g of a colourless, oily product. Purification of this by flash column chromatography on silica-gel, using pentane as the eluent, was accompanied by substantial decomposition, giving 1.1 g, (5.76 mmol, 39%) of *cis*-3-phenyl-2-trimethylsilylaziridine as a colourless, pungent smelling oil.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) -0.22 (6 H, s, Me<sub>3</sub>Si), 1.11 (1 H, s, NH), 1.34 (1 H, d, *J* 7.3 Hz, CHSiMe<sub>3</sub>), 3.40 (1 H, d, *J* 7.3 Hz, CHPh), 7.16-7.32 (5 H, m, Ph).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) -2.1 (Me<sub>3</sub>Si), 27.7 (CSi), 37.1 (CPh), 126.5, 127.4, 127.6 and 139.4

(Ph). M/e, 190 (26.8%, [M-H]<sup>+</sup>), 176 (5.8%, M<sup>+</sup>-CH<sub>3</sub>), 161 (7.5%, M<sup>+</sup>-2 x Me), 117 (10.5%), 105 (40.5%), 91 (16.9%), 77 (23.3%, Ph), 73 (100.0%, SiMe<sub>3</sub>), 59 (17.1%).

(ii) Trans-3-phenyl-2-trimethylsilylaziridine, [2.19]

In a modification of the method previously used by Duboudin<sup>8</sup>, *Trans*-3-phenyl-2-trimethylsilylaziridine was prepared in 91% yield using SS/RR-2-azido-1-bromo-2-phenyl-1-trimethylsilylethane, (3.6 g, 12.1 mmol) and lithium aluminium hydride (1.38 g, 36.3 mmol).  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 0.03 (9 H, s, Me<sub>3</sub>Si), 0.83 (1 H, s, NH), 1.13 (1 H, d, *J* 4 Hz, CHSiMe<sub>3</sub>), 2.80 (1 H, d, *J* 4 Hz, CHPh), 7.21 (5 H, s, Ph).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) -0.4 (Me<sub>3</sub>Si), 32.3 (CHSi), 35.4 (CHPh), 126.2, 127.2, 128.2 and 141.2 (Ph). No further analyses were obtained since this compound is reported in the literature.

(iii) Attempted reduction of bis(2-azido-1-bromoethyl)dimethylsilane; formation of dimethyl di(2-aminoethyl)silane

A mixture of products was obtained when bis(2-azido-1-bromoethyl)dimethylsilane was treated with lithium aluminium hydride. The major product had spectra consistent with dimethyl di(2-aminoethyl)silane. Further purification or separation was not attempted.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 1.02-1.40 (4 H, m, CH<sub>2</sub>Si), 2.90-3.25 (4 H, m, CH<sub>2</sub>N), 6.9-7.4 (4 H, m, H<sub>2</sub>N).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) -0.06, 0.23 (Me<sub>2</sub>Si), 16.8 (CSi), 36.2 (CN).

(iv) 2-Triphenylsilylaziridine

This was prepared using 2-azido-1-bromo-1-triphenylsilylethane (3.0 g, 7.35 mmol) and lithium aluminium hydride (0.75 g, 19.8 mmol). The white solid that was obtained crystallized from 2:5 chloroform-hexane yielding 1.98 g (6.58 mmol, 89.5%) 2-triphenylsilylaziridine as fine white plates which decomposed on heating.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 1.42 (1 H, d, *J* 7.2 Hz, CH<sub>2</sub>H<sub>b</sub>CH<sub>c</sub>), 1.64 (1 H, 't', *J* 6.4 Hz, CH<sub>a</sub>H<sub>b</sub>CH<sub>c</sub>), 1.88 (1 H, d, *J* 6.8 Hz, CH<sub>a</sub>H<sub>b</sub>CH<sub>c</sub>), 7.22-7.29 (10 H, m, Ph<sub>3</sub>Si), 7.52-7.61 (5 H, m, Ph<sub>3</sub>Si). The amino

proton was so broad that it was not observed, even at 400 MHz. The two methylene ring protons have a geminal coupling constant which is observed to be zero. However, they do couple with the proton on the adjacent carbon atom. The coupling constant which each methylene proton has with this proton is fairly similar in value. This  $^1\text{H}$  NMR spectrum differs from the spectra of other similarly substituted aziridines where the proton on the carbon bearing the silicon group resonates up field from the other two. There are two possible reasons for this change in pattern. The triphenylsilyl group is more deshielding than the trimethylsilyl group, shifting the proton on the  $\alpha$ -carbon down field. Also the proton which is *cis* to the triphenylsilyl group will experience considerably more deshielding (because of ring currents) than the *trans* proton. (With the trimethylsilyl substituted aziridines however, it is not possible to predict from the  $^1\text{H}$  NMR spectrum alone, which resonance is due to which  $\text{CH}_2$  proton).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) 15.2 ( $\text{CSi}$ ), 22.0 ( $\text{CN}$ ), 127.8, 129.5, 135.8 and 136.7 ( $\text{Ph}_3$ ).  $\nu_{\text{max}}$ . 3045, 2900, 1590, 1485, 1430, 1115, 855, 800, 730 and 700,  $\text{cm}^{-1}$ .  $\text{M/e}$  301 (8.2%,  $\text{M}^+$ ), 259 (12.0%,  $\text{SiPh}_3$ ), 182 (17.3%,  $\text{SiPh}_2$ ), 180 (24.3%), 105 (12.3%,  $\text{SiPh}$ ), 94 (24.5%,  $\text{PhN}^+\text{H}_3$ ), 73 (100.0%).

#### 6.4. Reductions of 2-azido-1-bromo-1-trimethylsilylhexane

2-Azido-1-bromo-1-trimethylsilylhexane was treated with a number of reducing agents with the aim of obtaining the corresponding aziridine, *trans*-3-butyl-2-trimethylsilyl-aziridine. Methods are described for the reactions with lithium aluminium hydride, K-selectride, sodium borohydride, calcium hydride and triphenylphosphine. A catalytic hydrogenation method is also described.

##### (i) With lithium aluminium hydride, synthesis of 2-amino-1-trimethylsilylhexane. [2.23]

Reduction of 2-azido-1-bromo-1-trimethylsilylhexane with lithium aluminium hydride according to the general method previously described for the reduction of RS/SR-2-azido-1-

bromo-2-phenyl-1-trimethylsilylhexane, resulted in the formation of 2-amino-1-trimethylsilylhexane in quantitative yield as a pale yellow oil.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) -0.04 (9 H, s,  $\text{Me}_3\text{Si}$ ), 0.68 (2 H, pair of d,  $J$  4.89 and 7.33 Hz,  $\text{CH}_2\text{Si}$ ,  $J_{\text{gem}}$  0), 0.86 (3 H, t,  $\text{CH}_3$ ), 1.05-1.76 (6 H, m,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 2.60-3.00 (2 H, br. s,  $\text{NH}_2$ ), 3.45-3.75 (1 H, m, CHN).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -1.1 ( $\text{Me}_3\text{Si}$ ), 13.6 ( $\text{CH}_3$ ), 22.3 ( $\text{CH}_2\text{Si}$ ), 26.2 ( $\text{CH}_2\text{CH}_3$ ), 28.0 ( $\text{CH}_2\text{CH}_2\text{CH}_3$ ), 40.7 ( $\text{CH}_2\text{CH}_2\text{CHNH}_2$ ), 48.3 ( $\text{CNH}_2$ ). The pair of doublets at 0.68 ppm and the multiplet at 3.45-3.75 in the  $^1\text{H}$  NMR spectrum confirm the regiochemical assignment. (The other regioisomer would lead to a pair of doublets of triplets, ignoring geminal coupling).

(ii) With K-selectride

K-selectride solution in THF (1M, 1.55 ml, 1.55 mmol) was added dropwise, under nitrogen to a stirring solution of the azide (0.43 g, 1.55 mmol) in 20 ml of dry THF at  $-5^\circ\text{C}$ . (The reaction was also carried out at a range of temperatures from  $-78^\circ\text{C}$  to room temperature, in each case similar results were obtained.) After 3 hours, saturated ammonium chloride (10 ml) was added with cooling and the mixture extracted with ether, dried and concentrated. Other work-up procedures included: hydrolysis with sodium bicarbonate solution, and purging with ammonia gas followed by aqueous work-up. The product mixture in each case was consistent with an aziridine or aziridinium species with a tri-*s*-butyl borane group coordinated to the nitrogen. Purification proved impossible and the procedure was abandoned.

(iii) With sodium borohydride

Sodium borohydride (0.76 g, 2 mmol) was added to a solution of 2-azido-1-bromo-1-trimethylsilylhexane, (0.83 g 3.0 mmol) in THF (20 ml). The suspension was heated to reflux and methanol (8 ml) was added dropwise over a 1 hour period with rapid stirring. The mixture was stirred for a further 17 hours at room temperature and then hydrolyzed by addition of 4 ml 1M hydrochloric acid and extracted with ether. Some decomposition of the



azide was observed when the product mixture was analysed by NMR spectroscopy.

Comparing the spectra of the product with those of the aziridine formed by method 6.4 (iv) indicated that no conversion to this compound had occurred.

(iv) With calcium hydride

2-Azido-1-bromo-1-trimethylsilylhexane, (0.60 g, 2.16 mmol), was dissolved in 10 ml THF. Calcium hydride (0.05 g, 1.20 mmol) was added and the mixture was stirred for 24 hours. The azide was recovered completely unreacted.

(v) By catalytic hydrogenation

The catalytic hydrogenation of this azide was attempted under a series of reaction conditions. The results are detailed in Table 6.1.

Table 6.1

Catalyst	Solvent	Conditions	Result
0.5% Pd/C	Ethanol	10% wt. catalyst 24 h	No reaction
5% Pd/C	Ethanol	10% wt. catalyst 6 h	Elimination of N <sub>3</sub> SiMe <sub>3</sub>
5% Pd/C	Ethyl acetate	10% wt. catalyst 24 h	No reaction
5% Pd/C	Hexane	10% wt. catalyst 24 h	No reaction
10% Pt/C	Ethyl acetate	5% wt. catalyst 24 h	No reaction
Lindlar	Ethanol	10% wt. catalyst 24 h	No reaction
Pd Black	Ethanol	5% wt. catalyst 24 h	No reaction

In each case the reactions were carried out at room temperature and atmospheric pressure with stirring. Hydrogen was introduced by a syringe needle, and in a separate set of experiments using a glass sinter. The reactions were followed by tlc and NMR spectroscopy.

(vi) With triphenylphosphine, synthesis of *trans*-3-butyl-2-trimethylsilylaziridine, [2.30]

To a solution of 2-azido-1-bromo-1-trimethylsilylhexane (0.28 g, 1.01 mmol) in THF (4 ml) was added triphenylphosphine (0.22 g, 1.10 mmol). The resulting yellow mixture was heated to 50 °C and stirred rapidly for 1.5 hours. On cooling to room temperature, 5 ml of 2*M* sodium hydroxide were added followed by stirring for 1 hour. The mixture was extracted with ether, dried and concentrated. On addition of hexane a white solid precipitated, leaving a yellow oil. The oil was separated from the solid and purified by flash column chromatography to give *trans*-3-butyl-2-trimethylsilylaziridine as a colourless oil (0.13 g, 0.765 mmol, 76%). The low coupling constant observed for the ring protons confirms the stereochemical assignment.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) -0.05 (9 H, s, Me<sub>3</sub>Si), 0.63 (1 H, d, *J* 4.6 Hz, CHSi), 0.69-1.57 (9 H, m, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.61-2.85 (1 H, m, NCHCH<sub>2</sub>).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) -3.3 (Me<sub>3</sub>Si), 14.1 (CH<sub>3</sub>), 22.7 (CH<sub>3</sub>CH<sub>2</sub>), 26.5 (CHSi), 30.2 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 34.6 (NCHCH<sub>2</sub>), 37.5 (NCHCH<sub>2</sub>).  $\nu_{\text{max}}$ . 3000-2850, 1710, 1455, 1245, 1100 and 870-820 cm<sup>-1</sup>. *M/e* 172 (100.0%, [M+H]<sup>+</sup>), 128 (5%), 100 (12%), 98 (6%, M<sup>+</sup>-SiMe<sub>3</sub>).

6.5 Synthesis of trimethylsilylaziridines by the photochemical reaction of alkyl azidoformates with vinylsilanes

(i) 1-Carboethoxy-2-trimethylsilylaziridine, [2.31]

Ethyl azidoformate (3.4 g, 30 mmol) and vinyltrimethylsilane (1.5 g, 15 mmol) were placed in a quartz tube and irradiated at 254 nm for 48 hours using a medium pressure arc carousel (rayonet). The tube was then recharged with vinyltrimethylsilane (1.5 g, 15 mmol) and irradiated for a further 48 hours. The resultant yellow oil was purified by chromatography on a silica-gel column, using ether-pentane (1:20) as the eluent. Fractions were collected and analysed by tlc. The pure aziridine (3.6 g, 19.3 mmol, 64%) was obtained in the first fraction as a sweet smelling colourless oil.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 0.07 (9 H, s, Me<sub>3</sub>Si), 1.27 (3 H, t,

$J$  7.2 Hz, CH<sub>3</sub>), 1.65 (1 H, dd,  $J$  5.1 and 7.3 Hz, SiCH), 2.04 (1 H, dd,  $J$  5.1 and 1.2 Hz, CH<sub>a</sub>H<sub>b</sub>), 2.38 (1 H, dd,  $J$  7.2 and 1.2 Hz, CH<sub>a</sub>H<sub>b</sub>), 4.13 (2 H, q,  $J$  7.2 Hz, OCH<sub>2</sub>).  $\delta_C$  (CDCl<sub>3</sub>) 14.3 (CH<sub>2</sub>CH<sub>3</sub>), 28.1 (CHSi), 28.4 (CH<sub>2</sub>N), 62.2 (CH<sub>2</sub>CH<sub>3</sub>), 164.2 (C=O).

(ii) Trans-3-butyl-1-carboethoxy-2-trimethylsilylaziridine. [2.32]

*Trans*-1-trimethylsilylhex-1-ene (6.24 g, 40 mmol) was placed in a quartz tube for irradiation. Ethyl azidoformate was added over eight days in four equal portions of 1.15 g (10 mmol), during the irradiation process. Hexane (10 ml) was added to the resultant yellow oil effecting precipitation of a white solid. The mixture was filtered and the mother liquor concentrated to give a pale yellow oil. This was purified by chromatography on silica-gel, using hexane as the eluent. The fractions were analysed by NMR spectroscopy. Residual alkene was collected in the early fractions. Later fractions yielded the pure aziridine as a colourless, faintly sweet smelling oil (4.1 g, 24.0 mmol, 60%).  $\delta_H$  (CDCl<sub>3</sub>) 0.06 (9 H, s, Me<sub>3</sub>Si), 0.91 (3 H, t, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 0.77 (1 H, d,  $J$  6.3 Hz, CHSi), 1.12-1.53 (9 H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub> and CH<sub>3</sub>CH<sub>2</sub>O), 2.04-2.34 (1 H, m, CH<sub>2</sub>CHN), 4.12 (2 H, q, OCH<sub>2</sub>).  $\delta_C$  (CDCl<sub>3</sub>) -2.9 (Me<sub>3</sub>Si), 14.0 (CH<sub>3</sub>), 14.4 (CH<sub>3</sub>), 22.4 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 29.4 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 33.2 (NCHCH<sub>2</sub>), 35.2 (CHSi), 40.3 (CHCH<sub>2</sub>), 61.9 (CH<sub>2</sub>O), 163.0 (C=O). Found: C, 59.23; H, 10.40; N, 5.24%, C<sub>12</sub>H<sub>25</sub>NO<sub>2</sub>Si requires: C, 59.21; H, 10.35; N, 5.75%.  $M/e$ , 244 (13.7%, [M+H]<sup>+</sup>), 228 (26.6%, M<sup>+</sup>-CH<sub>3</sub>), 214 (22.2%, [M<sup>+</sup>+H]), 198 (12.1%, M<sup>+</sup>-C<sub>4</sub>H<sub>9</sub>), 170 (89.7%, M<sup>+</sup>-CO<sub>2</sub>Et or SiMe<sub>3</sub>), 156 (13.4%), 142 (24.1%), 128 (11.2%), 114 (15.8%), 103 (21.2%), 73 (100.0%, SiMe<sub>3</sub> or CO<sub>2</sub>Et), 59 (44.4%).

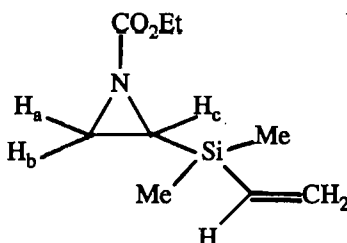
(iii) 1-Carbomethoxy-2-trimethylsilylaziridine. [2.33]

Vinyltrimethylsilane (1.0 g, 10.0 mmol) and methyl azidoformate (1.01 g, 10 mmol) were irradiated continuously for 24 hours in a quartz tube. The resultant mixture was evaporated and purified by chromatography on silica with pentane as the eluent. The product, 1-carbomethoxy-2-trimethylsilylaziridine was obtained as a colourless oil (0.55 g, 2.49

mmol, 24.9%). This was fairly volatile and so could not be purified sufficiently for elemental analysis in this way. An attempted distillation resulted in decomposition of the product.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) -0.062 (9 H, s,  $\text{Me}_3\text{Si}$ ), 1.55 (1 H, dd,  $J$  7.33 and 5.12 Hz,  $\text{CHSi}$ ), 1.93 (1 H, dd,  $J$  1.22 and 3.9 Hz,  $\text{CH}_a\text{H}_b$ ), 2.27 (1 H, dd,  $J$  1.22 and 7.33 Hz,  $\text{CH}_a\text{H}_b$ ), 3.73 (3 H, s,  $\text{OCH}_3$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -3.3 ( $\text{Me}_3\text{Si}$ ), 28.3 ( $\text{CSi}$ ), 28.6 ( $\text{CH}_2$ ), 53.4 ( $\text{OCH}_3$ ), 164.8 ( $\text{C=O}$ ).

(iv) 1-Carboethoxy-2-(dimethylvinylsilyl)aziridine. [2.34]

Divinyldimethylsilane (2.0 g, 17.9 mmol) and ethyl azidoformate (2.1 g, 18.3 mmol) were irradiated continuously for 4 days in a quartz tube. The resultant mixture was evaporated and purified by chromatography on silica with pentane as the eluent. The product, 1-carboethoxy-2-(dimethylvinylsilyl)aziridine was obtained as a clear oil (1.9 g, 9.55 mmol, 53%). NMR spectroscopy shows that the product is a mixture of diastereoisomers which are present in roughly equal amounts.



$\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) -0.021 and 0.010 (2 x 3 H, 2 x s,  $\text{Me}_2\text{Si}$ ), 1.11 (3 H, t,  $\text{CH}_2\text{CH}_3$ ), 1.55 (1 H, dd  $J$  7.33 and 5.13 Hz,  $\text{H}_c$ ), 1.92 (1 H, dd  $J$  1.22 and 5.13 Hz,  $\text{H}_a$ ), 2.23 (1 H, dd,  $J$  1.22 and 7.08 Hz,  $\text{H}_b$ ), 3.97 (2 H, q,  $\text{CH}_2$ ), 5.74-6.04 (3 H, m,  $\text{HC=CH}_2$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -5.3 and -5.0 ( $\text{Me}_2\text{Si}$ ), 14.3 ( $\text{CH}_3$ ), 26.9 ( $\text{CSi}$ ), 28.2 ( $\text{NCH}_2$ ), 62.0 ( $\text{CH}_2\text{CH}_3$ ), 133.8 ( $\text{HC=CH}_2$ ), 135.7 ( $\text{H}_2\text{C=CH}$ ), 163.8 ( $\text{C=O}$ ).  $M/e$  200 (18.6%,  $[\text{M}+\text{H}]^+$ ), 173 (15.2%,  $[\text{M}+\text{H}]^+-\text{H}_2\text{C=CH}^+$ ), 172 (35.9%,  $\text{M}^+-\text{H}_2\text{C=CH}^+$ ), 126 (42.7%,  $\text{M}^+-\text{CO}_2\text{Et}$ ), 112 (25.9%), 103 (44.2%), 100 (70.0%,  $\text{M}^+-\text{CH}_2\text{CHSiMe}_3$ ), 87 (19.7%), 86 (42.1%,  $\text{CH}_2\text{CHSiHMe}_2$ ), 85 (69.7%,  $\text{CH}_2\text{CHSiMe}_2^+$ ), 75 (41.1%), 73 (26.6%,  $\text{CO}_2\text{Et}$ ), 71

(27.2%), 59 (100.0%). Calculated M-CH<sub>3</sub>, 184.0794; measured M-CH<sub>3</sub>, 184.0708, calculated CO<sub>2</sub>Et, 126.0375; measured CO<sub>2</sub>Et, 126.0352.

(v) Bis(1-carboethoxyaziridin-2-yl)dimethylsilane, [2.35]

1-Carboethoxy-2-(dimethylvinylsilyl)aziridine (1.2 g, 6.0 mmol) and ethyl azidoformate (0.69 g, 6.0 mmol) were irradiated in a quartz tube for 48 hours. The product oil was purified by chromatography on silica. The column was eluted with neat hexane until all of the residual alkene had been collected before increasing the polarity gradually (up to 20% diethyl ether). Bis(1-carboethoxyaziridin-2-yl)dimethylsilane was obtained in the later fractions as a colourless oil (0.5 g, 0.174 mmol, 28.9%). The product is present as a mixture of diastereoisomers as indicated by the <sup>13</sup>C NMR spectrum; two distinct resonances are observed carbamate methyl groups and also, the ring carbons adjacent to silicon.  $\delta_C$  (CDCl<sub>3</sub>) 0.00 (Me<sub>2</sub>Si), 14.03 (2 x CH<sub>2</sub>CH<sub>3</sub>), 25.74 and 26.02 (CHSiMe<sub>2</sub>), 28.49 (CH<sub>2</sub>N), 62.50 (CH<sub>2</sub>O), 164.12 (C=O). Found: C, 49.67; H, 7.89; N, 9.26 %, C<sub>12</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub>Si requires: C, 50.32; H, 7.47; N, 9.78%. M/e 287 (17.9%, [M+H]<sup>+</sup>), 271 (4.7%, M<sup>+</sup>-Me), 246 (15.4%), 172 (100.0%, [M-EtO<sub>2</sub>CNCH<sub>2</sub>CH<sub>2</sub>]<sup>+</sup>), 103 (22.6%), 100 (60.1%), 85 (17.1%), 75 (23.7%) 59 (28.4%), 29 (81%, Et). Calculated M-CH<sub>3</sub>, 271.1114; measured M-CH<sub>3</sub>, 271.1111.

## 6.6 Synthesis of vinylsilanes by hydrosilylation of methyl propynoate

Two new vinylsilanes were prepared by the hydrosilylation of methyl propynoate with phenyldimethylsilane and diphenylmethylsilane using a method similar to that of Lukevics for the preparation of methyl 2-(triethylsilyl)propenoate, [2.6]<sup>4</sup>. The NMR spectra for these compounds were recorded at 400 Mz.

(i) Methyl 2-(dimethylphenylsilyl)propenoate, [2.7]

A catalytic amount (0.2 g) of 10% platinum on carbon (or hexachloroplatinic acid) was added to a stirring solution of dimethylphenylsilane (3.10 g, 22.8 mmol) and methyl

propynoate (1.92 g, 22.8 mmol). A mildly exothermic reaction was accompanied with weak effervescence. After 0.5 hours a substantial exotherm ensued accompanied by the development of a dark brown colour. The catalyst was removed by precipitation in hexane. The crude product comprised methyl 2-(dimethylphenylsilyl)propenoate (70%) the remainder being the *vicinal* adduct, *trans*-methyl 1-(dimethylphenylsilyl)propenoate. Pure methyl 2-(dimethylphenylsilyl)propenoate (3.2 g, 14.6 mmol, 64.2 %) was obtained by chromatography on silica, with hexane as the eluent. The product appeared in the later fractions.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.41 ( $\text{Me}_2\text{Si}$ ), 3.61 (3 H, s,  $\text{OCH}_3$ ), 5.92 (1 H, d,  $J$  2.93 Hz,  $\text{H}_a\text{H}_b\text{C=}$ ), 6.80 (1 H, d,  $J$  2.93 Hz,  $\text{H}_a\text{H}_b\text{C=}$ ), 6.796-6.803 and 7.29-7.50 (5 H, m, Ph).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -2.2 ( $\text{MeSi}$ ), 1.5 ( $\text{MeSi}$ ), 52.2 ( $\text{OMe}$ ), 128.4, 129.9 and 141.9 (Ph), 134.2 and 134.6 ( $\text{H}_2\text{C=}$  and  $\text{SiC=}$ ), 170.0 ( $\text{C=O}$ ). Found: C, 66.27; H, 7.45%,  $\text{C}_{12}\text{H}_{16}\text{O}_2\text{Si}$  requires: C, 65.41; H, 7.32%.

(ii) Methyl 2-(diphenylmethylsilyl)propenoate, [2.8]

This was prepared by the same method as for methyl 2-(dimethylphenylsilyl)propenoate. The product mixture consisted of 60% of the *geminal* isomer (methyl 2-(diphenylmethylsilyl)propenoate) and 40% of the *vicinal* isomer (*trans*-methyl 1-(diphenylmethylsilyl)propenoate). A hexane solution of this on cooling yielded a yellow solid; almost pure methyl 2-(diphenylmethylsilyl)propenoate was recovered from the mother liquor. Successive cooling of the mother liquor in stages yielded a yellow oil which was further purified by flash column chromatography.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.46 (3 H, s,  $\text{MeSi}$ ), 3.19 (3 H, s,  $\text{OCH}_3$ ), 5.53 (1 H, d,  $J$  1.20 Hz,  $\text{H}_a\text{H}_b\text{C=}$ ), 6.48 (1 H, d,  $J$  1.20 Hz,  $\text{H}_a\text{H}_b\text{C=}$ ), 6.70-7.20 (10 H, m,  $\text{Ph}_2\text{Si}$ ). Found C, 71.98; H, 6.49%,  $\text{C}_{17}\text{H}_{18}\text{O}_2\text{Si}$  requires: C, 72.30; H, 6.42%.

## 6.7 General procedure for the synthesis of aziridines by the thermolysis of phenyl azide in the presence of vinylsilanes

Aziridines were synthesized by the thermolysis of phenyl azide in the presence of: methyl 2-(triethylsilyl)propenoate, [2.6], methyl 2-(dimethylphenylsilyl)propenoate, [2.7], and methyl 2-(diphenylmethylsilyl)propenoate, [2.8] under an identical set of conditions. The NMR spectra for these compounds were recorded at 400 Mz. A general method is described for the synthesis of 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine.

### (i) 2-Carbomethoxy-1-phenyl-2-triethylsilylaziridine, [2.9]

A 60:40 mixture of methyl 2-(triethylsilyl)propenoate and *trans*-methyl 3-(triethylsilyl)propenoate (15 g, 45 mmol methyl 2-(triethylsilyl)propenoate) was heated to 110-120 °C in the presence of phenyl azide (5.35 g, 45 mmol). Heating was continued until evolution of nitrogen had subsided (*ca* 2 hours). All of the methyl 2-(triethylsilyl)propenoate reacted to give 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine and the *vicinal* alkene remained mostly unreacted. The residual alkene was removed by chromatography on silica, and the product aziridine purified by distillation (b.p., 110-117 °C, 0.1 mm) to give pure 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine (9.8 g, 31.5 mmol, 70%).  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) [0.68-0.84 (6 H, m); and 0.90-1.54 (9 H, m),  $\text{Et}_3\text{Si}$ ], 2.40 (1 H, d,  $J$  1.60 Hz,  $\text{NCH}_a\text{H}_b$ ), 2.76 (1 H, d,  $J$  1.60 Hz,  $\text{NCH}_a\text{H}_b$ ), 3.44 (3 H, s, OMe), 6.83-7.16 (5 H, m, Ph).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) 2.3 (3 x  $\text{CH}_2\text{Si}$ ), 7.9 (3 x  $\text{CH}_3\text{CH}_2\text{Si}$ ), 35.6 (NCSi), 36.9 ( $\text{CH}_2\text{N}$ ), 51.5 ( $\text{CH}_3\text{O}$ ), 120.6, 123.1, 128.5 and 150.7 (Ph), 172.0 ( $\text{C}=\text{O}$ ). Found: C, 65.75; H, 8.83; N, 4.51%,  $\text{C}_{16}\text{H}_{25}\text{NO}_2\text{Si}$  requires: C, 65.93; H, 8.65; N, 4.80%. Calculated M, 291.1655; measured M, 291.1699.

(ii) 2-Carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine. [2.10]

This was prepared using methyl 2-(dimethylphenylsilyl)propenoate (2.0 g, 80%, 7.27 mmol) and phenyl azide (0.87 g, 7.31 mmol) to give, after purification by column chromatography, pure 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine as a colourless viscous oil (2.0 g, 6.43 mmol, 88%).  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.30 and 0.38 (2 x 3 H, 2 x s,  $\text{Me}_2\text{Si}$ ), 2.22 (1 H, s,  $\text{NCH}_a\text{H}_b$ ), 2.67 (1 H, s,  $\text{NCH}_a\text{H}_b$ ), 3.21 (3 H, s,  $\text{OCH}_3$ ), 6.66-7.49 (10 H, m,  $\text{NPh}$  and  $\text{SiPh}$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -4.0 and -3.7 ( $\text{Me}_2\text{Si}$ ), 35.9 ( $\text{CSi}$ ), 38.1 ( $\text{CH}_2$ ), 51.8 ( $\text{CH}_3$ ), 120.8, 123.0, 128.4, 129.2, 129.7, 134.8, 136.6 and 150.8 ( $\text{CPh}$  and  $\text{NPh}$ ), 170.6 ( $\text{C=O}$ ).  $\nu_{\text{max}}$ . 3100-2810, d (1740, 1710), 1595, 1490, 1430, 1240, 1110, d (835, 815) and 700  $\text{cm}^{-1}$ . Found: C, 68.44; H, 6.86; N; 4.00%,  $\text{C}_{18}\text{H}_{21}\text{NO}_2\text{Si}$  requires: C, 69.41; H, 6.80; N, 4.50%.

(iii) 2-Carbomethoxy-2-diphenylmethylsilyl-1-phenylaziridine. [2.11]

Phenyl azide, heated in the presence of a mixture of isomeric alkene starting materials, probably resulted in unselective addition to give a mixture of aziridines which could not be separated by chromatography or distillation. The product mixture was too complex to analyse by NMR spectroscopy.

## 6.8 The reduction of 1-carboethoxy aziridines

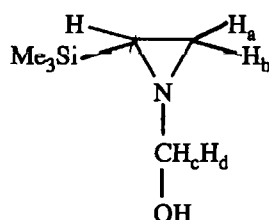
1-Carboethoxy-2-trimethylsilylaziridine and *trans*-3-butyl-1-carboethoxy-2-trimethylsilylaziridine were reduced with lithium aluminium hydride according to the general procedure described below for the reduction of 1-carboethoxy-2-trimethylsilylaziridine.

(i) 1-Hydroxymethyl-2-trimethylsilylaziridine. [2.36]

A solution of 1-carboethoxy-2-trimethylsilylaziridine (0.2 g, 1.07 mmol) in dry ether (3 ml) was added dropwise over a 10 minute period to a stirring slurry of lithium aluminium hydride (0.13 g, 3.42 mmol) in ether (20 ml) at 0 °C. The mixture was stirred for a further



1 hour at 0 °C and allowed to warm to room temperature to stir overnight. The grey coloured reaction mixture was again cooled to 0 °C and hydrolysed by dropwise addition of water (3 ml). The mixture was stirred rapidly for 30 minutes. The resultant white solid was washed with small portions of ether and the ethereal solution dried. The solvent was distilled from the product to give a pungent, pale yellow oil. This was further purified by flash column chromatography on silica, using pentane as the eluant, to give 1-hydroxymethyl-2-trimethylsilylaziridine as a clear oil, (0.091 g, 0.628 mmol, 59%). Since the product was volatile it was not possible to purify it sufficiently in this way for elemental analysis. An attempted short path distillation resulted in decomposition.



$\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) -0.09 (9 H, s,  $\text{Me}_3\text{Si}$ ), 0.53 and 0.58 (2 H, dd,  $J$  8.05 and 5.13 Hz,  $\text{CHSiMe}_3$ ), 1.45 (1 H, d,  $J$  8.05 Hz,  $\text{H}_a$ ), 1.57 (1 H, d,  $J$  5.13 Hz,  $\text{H}_b$ ), 3.59 (1 H, d,  $J$  7.81 Hz,  $\text{H}_c$ ), 3.8 (1 H, d,  $J$  7.81 Hz,  $\text{H}_d$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -3.7 ( $\text{Me}_3\text{Si}$ ), 25.8 ( $\text{CHSi}$ ), 28.7 ( $\text{CH}_2\text{CHSi}$ ), 85.8 ( $\text{CH}_2\text{OH}$ ).

(ii) *Trans*-3-butyl-2-trimethylsilylaziridine, [2,30]

Reduction of *trans*-3-butyl-1-carboethoxy-2-trimethylsilylaziridine with lithium aluminium hydride resulted in complete conversion to *trans*-3-butyl-2-trimethylsilylaziridine. No partially reduced intermediate could be detected even when moist ether was used.

$\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) -0.05 (9 H, s,  $\text{Me}_3\text{Si}$ ), 0.63 (1 H, d,  $J$  4.6 Hz,  $\text{CHSiMe}_3$ ), 0.69-1.57 (9 H, m,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ), 2.61-2.85 (1 H, m,  $\text{CHCH}_2$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -3.3 ( $\text{Me}_3\text{Si}$ ), 14.1 ( $\text{CH}_3$ ), 22.7 ( $\text{CH}_3\text{CH}_2$ ), 26.5 ( $\text{CHSi}$ ), 30.2 ( $\text{CH}_3\text{CH}_2\text{CH}_2$ ), 34.6 ( $\text{NCHCH}_2$ ), 37.5 ( $\text{NCHCH}_2$ ).  $\nu_{\text{max}}$ . 2805-3000, 1710, 1455, 1245, 1100 and 820-870  $\text{cm}^{-1}$ .  $M/e$  172 (100.0%,  $[\text{M}+\text{H}]^+$ ), 128 (5%), 100 (12%), 98 (6%,  $\text{M}^+-\text{SiMe}_3$ ).

## 6.9 Reaction of *trans*-3-butyl-1-carboethoxy-2-trimethylsilylaziridine with butyllithium

To a stirred solution of the aziridine (0.20 g, 0.823 mmol) in THF (20 ml) at -15 °C and under nitrogen, was added *n*-butyllithium (1.6M hexane solution, 1.03 ml, 1.65 mmol). The mixture was stirred for 1 hour at -15 °C and allowed to warm slowly to room temperature to stir overnight. Hydrolysis by pouring into ammonium chloride solution was followed by extraction with ether, drying and evaporation of the solvent. NMR spectroscopy indicated (by comparison with an authentic sample) that 5-nonanone had been produced quantitatively along with a new silicon-containing species. The two compounds failed to separate by chromatography so no further attempts were made to isolate them. A similar result, i.e., the production of 5-nonanone was observed when 1-carboethoxy-2-trimethylsilylaziridine was treated with *n*-butyllithium.

## 6.10 Ring opening of silylaziridines in CDCl<sub>3</sub> with gaseous hydrogen halides

### (i) Ring opening of *cis*-3-phenyl-2-trimethylsilylaziridine with hydrogen chloride, formation of 2-amino-1-chloro-2-phenyl-1-trimethylsilylethane hydrochloride, [3.27]

*Cis*-3-phenyl-2-trimethylsilylaziridine (0.1 g, 0.524 mmol) was placed in a 5 ml NMR tube with 1 ml CDCl<sub>3</sub> and hydrogen chloride gas was passed through the solution. After 1 second of purging, the NMR spectrum of the reaction mixture indicated the presence of an aziridinium salt and also that of a ring opened product. After several seconds of purging with the gas, the product consisted entirely of the ring opened derivative. The solvent was evaporated and the remaining off-white solid was recrystallized from 50:50, ether:chloroform to give white crystals of 2-amino-1-chloro-2-phenyl-1-trimethylsilyl-

ethane hydrochloride (0.133 g, 0.504 mmol, 96.2%). The solid decomposed without melting on heating.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) -0.18 (9 H, s,  $\text{Me}_3\text{Si}$ ), 3.85 (1 H, d,  $J$  10.5 Hz,  $\text{CHSi}$ ), 4.28 (1 H, d,  $J$  10.5 Hz,  $\text{CHPh}$ ), 6.33 (3 H, s,  $\text{NH}_3$ , exchangeable with  $\text{D}_2\text{O}$ ), 7.25 - 7.40 (5 H, m, Ph).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -3.0 ( $\text{Me}_3\text{Si}$ ), 51.2 ( $\text{CSiMe}_3$ ), 61.0 ( $\text{CPh}$ ), 128.8, 129.4, 130.0 and 133.9 (Ph).

(ii) Ring opening of *trans*-3-butyl-2-trimethylsilylaziridine with hydrogen bromide, formation of 2-amino-1-bromo-1-trimethylsilylhexane hydrobromide.

The reaction was carried out as before using 0.2 g of *trans*-3-butyl-2-trimethylsilylaziridine and gaseous hydrogen bromide. The proton NMR spectrum of the product obtained from the reaction is consistent with 2-amino-1-bromo-1-trimethylsilylhexane hydrobromide. An attempt to purify this product further resulted in decomposition.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.24 (9 H, s,  $\text{Me}_3\text{Si}$ ), 1.62-1.95 (9 H, m,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ), 4.00 (1 H, d,  $J$  2 Hz,  $\text{CHBr}$ ), 4.36 (1 H, dt,  $J$  2.0 and 6.2 Hz,  $\text{CHN}$ ), 7.92 (3 H, s,  $\text{NH}_3$ ).

(iii) Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with hydrogen chloride ethyl *N*-(2-chloro-2-trimethylsilylethyl) carbamate hydrochloride

1-Carboethoxy-2-trimethylsilylaziridine (0.3 g, 1.60 mmol) was placed in a 5 mm NMR tube with 1 ml of deuteriochloroform and the tube cooled in an ice bath. Hydrogen chloride was passed through the solution until all of the aziridine had been consumed, the reaction being followed by proton NMR spectroscopy. On evaporation of the solvent, a brown oil was obtained which was purified by column chromatography on silica using 3:10 ether-hexane as the eluant. A colourless oil was obtained which was insoluble in hexane. This yielded, after several recrystallization steps, pure, well defined crystals of the ring opened product, ethyl *N*-(2-chloro-2-trimethylsilylethyl) carbamate hydrochloride (0.23 g, 0.885 mmol, 55%).  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) -0.008 (9 H, s,  $\text{Me}_3\text{Si}$ ), 1.08 (3 H, t,  $\text{CH}_3$ ), 3.10-3.96 (3 H, m,  $\text{CH}_2\text{CH}$ ), 5.02 (2 H, br. s, HN).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -3.5 ( $\text{Me}_3\text{Si}$ ), 14.6 ( $\text{CH}_3$ ), 44.3 ( $\text{CSi}$ ),

51.4 (CN), 60.9 (CH<sub>2</sub>O), 156.4 (C=O). Found: C, 36.77; H, 6.79; N, 5.25, C<sub>8</sub>H<sub>19</sub>NO<sub>2</sub>SiCl<sub>2</sub> requires: C, 36.92; H, 7.36; N, 5.38.

(iv) Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with hydrogen bromide, formation of ethyl *N*-(2-bromo-2-trimethylsilylethyl) carbamate, [3.11]

This reaction was carried out using the same procedure as for the ring opening reaction of 1-carboethoxy-2-trimethylsilylaziridine with hydrogen chloride to give the ring opened carbamate product, [3.11] in 52% yield.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 0.11 (9 H, s, Me<sub>3</sub>Si), 1.21 (3 H, t, CH<sub>3</sub>), 3.24-3.80 (3 H, m, CH<sub>2</sub>CHSi), 4.09 (2 H, q, CH<sub>2</sub>O), 7.12 (1 H, br. s, HN).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) -3.2 (Me<sub>3</sub>Si), 14.4 (CH<sub>3</sub>), 43.7 (CSi), 44.0 (CH<sub>2</sub>N), 60.8 (CH<sub>2</sub>O), 156.2 (C=O). Found: C, 35.88; H, 6.78; N, 5.22; Br, 29.1%, C<sub>8</sub>H<sub>18</sub>NO<sub>2</sub>SiBr requires: C, 35.82; H, 6.76; N, 5.22; Br, 29.79%.

(v) Reaction of 2-carboethoxy-1-phenyl-2-triethylsilylaziridine with hydrogen chloride

2-Carboethoxy-1-phenyl-2-triethylsilylaziridine (0.1 g, 0.00343 mmol) was dissolved in 1 ml dry ether and hydrogen chloride was passed through the solution for a few seconds. The mixture was evaporated leaving a brown oil. This was purified by column chromatography using 10:1 pentane-ether as the eluant. The only product which could be recovered was a white solid which could be identified as aniline hydrochloride by NMR spectroscopy.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 4.9 (3 H, br. s, NH<sub>3</sub>), 7.2-7.3 (5 H, s, Ph).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) 124.1, 130.2, 131.2, 131.9.

(vi) Reaction of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with hydrogen chloride

This reaction was carried out as in 6.5 (v) giving again, aniline hydrochloride as the major product.

### 6.11 Reaction of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with 1M hydrogen chloride solution in ether

To a solution of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine (0.1 g, 0.32 mmol) in dry ether (5 ml) was added a commercially prepared, 1M solution of hydrogen chloride in ether (0.32 ml, 0.32 mmol) and the solution stirred for 0.5 hours. The solvent was evaporated to leave a yellow oil whose NMR spectra indicated the presence of several compounds, including aniline hydrochloride. A major product was thought be the ring opened species as suggested by the carbon NMR spectrum.  $\delta_C$  (CDCl<sub>3</sub>) -4.9 and -4.7 (SiMe<sub>2</sub>), 50.1 (MeO), 52.8 (CH<sub>2</sub>N), 65.2 (CCl), 113.9, 118.6, 128.9 and 147.4, (NPh and SiPh), 171.3 (C=O).

### 6.12 Ring opening of silylaziridines with trimethylsilyl halides

The same method was applied to the ring opening reactions of 1-carboethoxy-2-trimethylsilylaziridine with trimethylsilyl bromide, trimethylsilyl iodide, and trimethylsilyl chloride. *Trans*-3-butyl-1-carboethoxy-2-trimethylsilylaziridine was also treated with trimethylsilyl halides giving rise to complex mixtures which were not further analysed. The general method is described for the reaction of 1-carboethoxy-2-trimethylsilylaziridine with trimethylsilyl bromide.

#### (i) Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with trimethylsilyl bromide, formation of ethyl *N*-(2-bromo-2-trimethylsilylethyl) *N*-trimethylsilylcarbamate

1-Carboethoxy-2-trimethylsilylaziridine (0.1 g, 0.535 mmol) was placed in a 5 mm NMR tube with dry deuterochloroform, under nitrogen and the tube was cooled in an ice bath. Trimethylsilyl bromide (0.082 g, 0.0707 ml, 0.535 mmol) was syringed slowly into the sealed tube. An attempt to purify the product resulted in decomposition, however, NMR spectra indicated that almost complete conversion to the  $\alpha$ -ring opened product, ethyl *N*-(2-bromo-2-trimethylsilylethyl) *N*-trimethylsilylcarbamate had been achieved.

$\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) -0.04 (9 H, s,  $\text{Me}_3\text{SiC}$ ), 0.07 (9 H, s,  $\text{Me}_3\text{SiN}$ ), 1.17 (3 H, t,  $\text{CH}_3$ ), 3.00-3.85 (3 H, m,  $\text{CH}_2\text{CH}$ ), 4.06 (2 H, q,  $\text{CH}_2$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -3.2 ( $\text{Me}_3\text{SiC}$ ), 0.5 ( $\text{Me}_3\text{SiN}$ ), 14.3 ( $\text{CH}_3$ ), 22.5 ( $\text{CBr}$ ), 47.3 ( $\text{CH}_2\text{N}$ ), 60.8 ( $\text{CH}_2\text{O}$ ), 158.4 ( $\text{C=O}$ ).

(ii) Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with trimethylsilyl iodide formation of ethyl *N*-(2-iodo-2-trimethylsilylethyl) *N*-trimethylsilylcarbamate

This reaction was carried out as before using 1-carboethoxy-2-trimethylsilylaziridine (0.1 g, 0.535 mmol) and trimethylsilyl iodide (0.107 g, 0.0761 ml, 0.535 mmol). Again, almost complete conversion to the ring opened product, ethyl *N*-(2-iodo-2-trimethylsilylethyl) *N*-trimethylsilylcarbamate was achieved, but this could not be purified further.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.26 (9 H, s,  $\text{Me}_3\text{SiC}$ ), 0.41 (9 H, s,  $\text{Me}_3\text{SiN}$ ), 1.36 (3 H, t,  $\text{CH}_3$ ), 3.05-3.40 (2 H, m,  $\text{CH}_2\text{N}$ ), 4.02 (2 H, q,  $\text{CH}_2\text{O}$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -2.3 ( $\text{Me}_3\text{SiC}$ ), 0.7 ( $\text{Me}_3\text{SiN}$ ), 14.2 ( $\text{CH}_3\text{CH}_2$ ), 21.8 ( $\text{CH}_3$ ), 47.4 ( $\text{NCH}_2$ ), 60.7 ( $\text{OCH}_2$ ), 157.2 ( $\text{C=O}$ ). The low chemical shift of the carbon bearing the iodine is due to the heavy atom effect of the iodine atom. In the  $^1\text{H}$  NMR spectrum the multiplet at 3.05-3.40 cannot be further analysed due to the presence of ethyl iodide which is formed as a by-product.

(iii) Reaction of 1-carboethoxy-2-trimethylsilylaziridine with trimethylsilyl chloride, formation of ethyl *N*-(2-chloro-2-trimethylsilylethyl) carbamate hydrochloride

This reaction was carried out as before using 1-carboethoxy-2-trimethylsilylaziridine (0.1 g, 0.535 mmol) and trimethylsilyl chloride (0.058 g, 0.068 ml, 0.535 mmol). However, the reaction was much slower. Treatment of 1-carboethoxy-2-trimethylsilylaziridine with trimethylsilyl chloride for several months eventually led to the formation of the hydrogen chloride ring opened product as determined by comparison of the NMR spectra with those of an authentic sample.

### 6.13 Ring opening of silylaziridines with trifluoroacetic acid

These reactions were carried out at  $-11^{\circ}\text{C}$  (ice/methanol) under nitrogen, either in dry deuteriochloroform in a 5 mm NMR tube, or in dry ether with stirring. Neat, pre-cooled trifluoroacetic acid was added to the aziridine solution. The products began to decompose on exposure to air and so could not be isolated in a pure form.

#### (i) Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with trifluoroacetic acid, formation of ethyl *N*-(2-trifluoroacetato-2-trimethylsilylethyl) carbamate

The reaction was carried out using 0.1 g (0.535 mmol) 1-carboethoxy-2-trimethylsilylaziridine and 0.6 g (0.04 ml, 0.535 mmol) trifluoroacetic acid leading quantitatively (by NMR spectroscopy) to the ring opened product, ethyl *N*-(2-trifluoroacetato-2-trimethylsilylethyl) carbamate.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.07 (9 H, s,  $\text{Me}_3\text{Si}$ ), 1.23 (3 H, t,  $\text{CH}_3$ ), 3.41 (1H, d,  $J$  8.30 Hz,  $\text{NCH}_a\text{H}_b$ ), 3.49 (1H, d,  $J$  4.88 Hz,  $\text{NCH}_a\text{H}_b$ ), 4.06 (2 H, t,  $\text{CH}_2\text{CH}_3$ ), 4.99 (1 H, dd,  $J$  8.30 Hz and 4.88 Hz,  $\text{CHSiMe}_3$ ), 5.90 (1 H, br s, NH).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -4.2 ( $\text{Me}_3\text{Si}$ ), 14.2 ( $\text{CH}_3$ ), 41.7 ( $\text{NCH}_2$ ), 61.1 ( $\text{CH}_2\text{CH}_3$ ), 74.2 (CSi), 119.4 (q,  $\text{CF}_3$ ), 156.8 (C=O).  $M/e$  301 (0.2%,  $M^+$ ), 229 (2.9%)/230/231 (9:2:1,  $M^+$ - $\text{SiMe}_3$  or  $\text{CO}_2\text{Et}$ ), 188 (1.9%,  $M^+$ - $\text{O}_2\text{CCF}_3$ ), 116 (44.9%)/117/118 (9:2:1), 101 (83.2%)/102/103 (77:11:7), 73 (86.8%,  $\text{SiMe}_3$  or  $\text{CO}_2\text{Et}$ ), 69 (55.6%)/70/71 (88:6:5,  $\text{CF}_3$ ), 59 (38.6), 29 (100.0%, Et). Second order effects are observed in the proton NMR spectrum due to the similar chemical shifts of  $\text{H}_a$  and  $\text{H}_b$ . No geminal coupling constant could therefore be measured.

#### (ii) Reaction of 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine with trifluoroacetic acid formation of methyl 2-anilino-1-trifluoroacetato-1-triethylsilyl propanoate

The reaction was carried out using 0.11 g, (0.378 mmol) 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine and 0.043 g, (0.378) mmol trifluoroacetic acid. The major product from this reaction was the ring opened species, methyl 2-anilino-1-trifluoroacetato-1-

triethylsilyl propanoate which began to decompose within a few hours.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.56-0.62 [6 H, m] and 0.9-1.0 [9 H, m] ( $\text{SiEt}_3$ ), 2.49 (1 H, s,  $\text{NCH}_a\text{H}_b$ ), 2.84 (1 H, s,  $\text{NCH}_a\text{H}_b$ ), 3.45 (3 H, s,  $\text{CH}_3$ ), 6.85-7.29 (5 H, m, Ph).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ), 3.2 (3 x  $\text{SiCH}_2\text{CH}_3$ ), 7.9 (3 x  $\text{SiCH}_2\text{CH}_3$ ), 35.9 ( $\text{NCH}_2$ ), 52.7 ( $\text{CH}_3$ ), 73.4 ( $\text{COCOCF}_3$ ), 120.9, 123.6, 128.7 and 148.1 (Ph), 171.2 ( $\text{C=O}$ ). The geminal coupling constant is observed to be zero.

(iii) Reaction of 1-phenyl-2-trimethylsilylaziridine with trifluoroacetic acid, formation of *N*-phenyl *N*-(2-trifluoroacetato-2-trimethylsilylethyl) amine

This reaction was carried out as before using 0.2 g (1.05 mmol), 1-phenyl-2-trimethylsilylaziridine and 0.12 g (1.05 mmol), trifluoroacetic acid to give almost quantitatively by NMR, the  $\alpha$ -ring opened product, *N*-phenyl *N*-(2-trifluoroacetato-2-trimethylsilylethyl) amine.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.09 (9 H, s,  $\text{Me}_3\text{Si}$ ), 3.68-3.78 (2 H, m,  $\text{NCH}_2$ ), 5.39 (1 H, dd,  $J$  3.22 and 9.08 Hz,  $\text{CHSi}$ ), 7.43 (5 H, s, Ph), 11.10 (1 H, s, NH).

#### 6.14 Ring opening of silylaziridines with trifluoromethanesulphonic acid

These reactions were carried out on a small scale by a general method which is described for the reaction with 2-dimethylphenylsilyl-2-carbomethoxy-1-phenylaziridine. All of the products decomposed on exposure to air and so no pure products could be isolated.

(i) Reaction of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with trifluoromethanesulphonic acid, formation of methyl 2-anilino propenoate, [3.30]

2-Carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine, (0.05 g, 0.161 mmol) was dissolved under nitrogen in 0.5 ml of deuteriochloroform, in a 5 mm NMR tube, and cooled in an ice/methanol bath. Trifluoromethanesulphonic acid (0.0241 g, 0.161 mmol) was syringed slowly into the tube. The reaction was followed by NMR spectroscopy and



complete conversion to methyl 2-anilinopropenoate was observed after 2 hours.

$\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 3.89 (3 H, s, Me), 5.86 (1 H, d,  $J$  3.42 Hz,  $\text{H}_a\text{H}_b\text{C}=\text{C}$ ), 6.34 (1 H, d,  $J$  3.42 Hz,  $\text{H}_a\text{H}_b\text{C}=\text{C}$ ), 7.41-7.65 (5 H, m, Ph).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) 54.0 ( $\text{CH}_3$ ), 114.8, 118.2, 128.9, 129.1, 132.4 and 134.1 (NPh and  $\text{C}_{\text{Ph}}$ ), 160.7 ( $\text{C}=\text{O}$ ).

(ii) Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with trifluoromethanesulphonic acid, formation of ethyl *N*-(2-triflate-2-trimethylsilylethyl) carbamate, [3.28a]

The reaction was carried out using 0.1 g (0.535 mmol) 1-carboethoxy-2-trimethylsilylaziridine and 0.047 ml, (0.535 mmol) trifluoromethanesulphonic acid. NMR spectroscopy indicated immediate and quantitative conversion to ethyl *N*-(2-triflate-2-trimethylsilylethyl) carbamate, [3.28a].  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.12 (9 H, s,  $\text{Me}_3\text{Si}$ ), 1.39 (3 H, t,  $\text{CH}_3$ ), 3.78 (1 H, dd,  $J$  9.76 and  $J$  12.21 Hz,  $\text{NH}_a\text{H}_b$ ), 4.16 (1 H, dd  $J$  9.67 and  $J$  10.74,  $\text{NH}_a\text{H}_b$ ), 4.57 (2 H, q,  $\text{CH}_2\text{CH}_3$ ), 5.01 (1 H, dd,  $J$  12.21 Hz and  $J$  10.74 Hz,  $\text{CHSi}$ ), 9.96 (1 H, s, NH).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -5.2 ( $\text{Me}_3\text{Si}$ ), 13.7 ( $\text{CH}_3$ ), 45.2 ( $\text{NCH}_2$ ), 72.9 ( $\text{CH}_2\text{CH}_3$ ), 81.9 ( $\text{CSi}$ ), 119.6 (q,  $\text{CF}_3$ ), 165.7 ( $\text{C}=\text{O}$ ).

## 6.15 Reactions of silylaziridines with methyl trifluoromethanesulphonic acid

A general method for the reactions of silylaziridines with methyl trifluoromethanesulphonic acid is described for 1-carboethoxy-2-trimethylsilylaziridine.

(i) Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with methyl trifluoromethanesulphonic acid, formation of ethyl *N*-(2-triflate-2-trimethylsilylethyl) *N*-methylcarbamate, [3.28b]

This reaction was carried out using 0.13 g (0.695 mmol) 1-carboethoxy-2-trimethylsilylaziridine and 0.115 g (0.079 ml, 0.695 mmol) methyl trifluoromethanesulphonic acid leading to the ring opened product in almost quantitative yield by NMR spectroscopy.

$\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.42 (9 H, s,  $\text{Me}_3\text{Si}$ ) 1.49 (3 H, t,  $\text{CH}_3$ ), 2.90 (3 H, s, NMe), 3.37 (1 H, d,  $J$  10.2 Hz,  $\text{NCH}_a\text{H}_b$ ), 3.39 (1 H, d,  $J$  7.1 Hz,  $\text{NCH}_a\text{H}_b$ ), 4.31 (2 H, q,  $\text{CH}_2\text{CH}_3$ ), 4.91 (2 H, dd,  $J$  7.1 Hz and  $J$  10.2 Hz,  $\text{CHSi}$ ). The geminal coupling constant is observed to be zero.  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -5.1 ( $\text{Me}_3\text{Si}$ ), 13.7 ( $\text{CH}_3$ ), 31.2 (MeN), 50.8 ( $\text{NCH}_2$ ), 72.7 ( $\text{CH}_2\text{CH}_3$ ), 79.6 ( $\text{CSi}$ ), 120.1 (q,  $\text{CF}_3$ ), 162.9 ( $\text{C=O}$ ).

(ii) Reaction of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with methyl trifluoromethanesulphonic acid

This reaction was carried out as before using 0.05 g (0.161 mmol) 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine and 0.026 g (0.018 ml, 0.160 mmol) methyl trifluoromethanesulphonic acid. The NMR spectra were fairly complex, but suggested that both the monoalkylated ring opened adduct, [3.32] and the dialkylated ring opened adduct [3.33] were major products.

6.16 Reaction of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with trimethylsilyl trifluoromethanesulphonic acid, formation of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenyl-1-trimethylsilylaziridinium trifluoromethanesulphonate

This reaction was carried out using 0.05 g (0.161 mmol) 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine, [3.29] and 0.036 g (0.031 ml, 0.161 mmol) trimethylsilyl trifluoromethanesulphonic acid. Complete conversion to 2-carbomethoxy-2-dimethylphenylsilyl-1-phenyl-1-trimethylsilylaziridinium trifluoromethanesulphonate, [3.31] was observed. The product could not be isolated owing to decomposition on exposure to air.

$\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.12 and 0.44 (6 H, 2 x s,  $\text{Me}_2\text{Si}$ ), 0.52 (9 H, s,  $\text{Me}_3\text{SiN}$ ), 2.53 (1 H, s,  $\text{NCH}_a\text{H}_b$ ), 2.94 (1 H, s,  $\text{NCH}_a\text{H}_b$ ), 3.51 (3 H, t,  $\text{CH}_3$ ), 6.84-7.59 (10 H, m, NPh and SiPh). The geminal coupling constant for the two ring protons is observed to be zero.  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -3.6 and -3.4 ( $\text{Me}_2\text{Si}$ ), 0.9 ( $\text{Me}_3\text{SiN}$ ), 36.5 ( $\text{CH}_2$ ), 39.8, ( $\text{CSi}$ ), 50.6 ( $\text{CH}_3\text{O}$ ),

121.3, 123.9, 128.4, 129.5, 130.1, 130.2, 135.0 and 149.37 (NPh and CPh), 170.9 (C=O).

#### 6.17 Ring opening of 1-carboethoxy-2-trimethylsilylaziridine with perchloric acid, formation of ethyl *N*-(2-hydroxy-2-trimethylsilyl-ethyl) carbamate

1-Carboethoxy-2-trimethylsilylaziridine, [3.4] (0.2 g, 1.07 mmol) was dissolved in 5 ml of ether and perchloric acid (0.179 g, 60%, 1.07 mmol) was added. The mixture was shaken vigorously for several minutes and then 2 ml sodium bicarbonate solution was added. The organic layer was dried and evaporated to yield 0.17 g (0.829 mmol, 77%) of the almost pure ethyl *N*-(2-hydroxy-2-trimethylsilyl-ethyl) carbamate as a colourless oil.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) -0.08 (9 H, s,  $\text{Me}_3\text{Si}$ ), 1.16 (3 H, t,  $\text{CH}_3$ ), 3.10-3.40 (3 H, m,  $\text{NCH}_2\text{CH}$ ), 4.04 (2 H, q,  $\text{OCH}_2\text{CH}_3$ ), 4.40 (1 H, br s, NH).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -3.7 ( $\text{Me}_3\text{Si}$ ), 14.8 ( $\text{CH}_3$ ), 45.0 ( $\text{NCH}_2$ ), 61.1 ( $\text{CH}_2\text{CH}_3$ ), 66.2 (CSi), 157.7 (C=O).  $M/e$  204 (26.2%,  $[\text{M}-\text{H}]^+$ ), 188 (30.5%,  $\text{M}^+-\text{OH}$ ), 162 (24.1%), 147 (18.2%), 146 (27.7%), 132 (18.7%,  $\text{M}^+-\text{SiMe}_3$  or  $\text{CO}_2\text{Et}$ ), 116 (36.3%), 101 (54.1%), 73 (100.0%,  $\text{SiMe}_3$ ).

#### 6.18 The reaction of silylaziridines with fluoride ion in the presence or absence of electrophiles

A broad series of reactions was performed exploring the reactions of silylaziridines with fluoride ion, both in the absence, and in the presence of electrophiles (such as aldehydes or ketones). The results of the study are reported in Tables 6.2, 6.3, 6.4. and 6.5.

Different sources of fluoride ion were used including alkali metal fluorides, TAS fluoride, and tetrabutylammonium fluoride. Various sources of tetrabutylammonium fluoride were used including the crystalline trihydrate form, a 5% aqueous 1M solution in THF and tetrabutylammonium fluoride supported on silica gel. With some reactions, another agent was included in an attempt to promote the reaction of fluoride with the aziridines. These

were tetraphenylphosphonium bromide and the crown ether, 18-crown-6. Several methods were applied in an attempt to dry the sources of fluoride and these are described below.

1. Where a dried source of potassium fluoride was used, the fluoride was heated in an oven to 200 °C for 8 hours prior to use. From the oven it was transferred to a desiccator and used immediately.
2. Tetrabutylammonium fluoride was dried by two methods, A and B which are described below.

#### Method A

This method was used in order to dry commercial samples of tetrabutylammonium fluoride trihydrate, and is similar to that used by Cox<sup>9</sup>. Typically a sample (1.0 g) was heated with stirring at 40 °C under high vacuum for 48 hours. This method was effective in removing two equivalents of water as determined by weight loss.

#### Method B

This method was used to dry samples of commercial 1 M tetrabutylammonium fluoride in THF containing 5 wt% water. A 10 cm<sup>3</sup> teflon sealed vial was partially filled with 4 Å molecular sieves which had been dried by heating for 1 day in an oven at 200 °C and then in a vacuum oven at 90 °C for three days. The vial was then filled with the tetrabutylammonium fluoride solution. After several hours of shaking the liquid was quickly transferred into a second vial containing fresh, activated molecular sieves and shaken for 24 hours. The preparation was used within the next 24 hours. When used, the material was removed by syringe and transferred to the reaction vial.

#### Successful desilylation reactions

- (i) Preparation of 2-carbomethoxy-1-phenylaziridine, [4.25]

2-Carbomethoxy-1-phenylaziridine was the product obtained under various conditions when 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine or 2-carbomethoxy-2-dimethylphenyl-

silyl-1-phenylaziridine was reacted with fluoride ion in the presence or absence of electrophiles. The various conditions employed are detailed in tables 6.4 and 6.5. Isolation of the product was carried out in the following manner. The reaction mixture was diluted with ether and the solution washed with several portions of brine, in order to remove the fluoride source. The resultant solution was then dried and evaporated prior to purification by column chromatography on silica, hexane or pentane as the eluent. Pure aziridine was recovered in the later fractions.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 2.26 (1 H, dd,  $J$  1.46 Hz and 6.34 Hz,  $\text{CHCO}_2\text{Me}$ ), 2.63 (1 H, dd,  $J$  1.46 Hz and 2.91 Hz,  $\text{NCH}_a\text{H}_b$ ), 2.76 (1 H, dd,  $J$  6.34 Hz and 2.91 Hz,  $\text{NCH}_a\text{H}_b$ ), 3.74 ( $\text{OCH}_3$ ), 6.88-7.55 (5 H, m, Ph).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ), 33.7 ( $\text{CH}_2$ ), 37.5 ( $\text{CH}$ ), 52.1 ( $\text{OCH}_3$ ), 120.7, 123.4, 129.1 and 152.5 (Ph), 170.5 ( $\text{C}=\text{O}$ ).  $\nu_{\text{max}}$  3090-2835, 1745, 1595, 1490, 1300-1250, 1200, 1120, 1195, 1005, 910, 840, 795 and  $700\text{ cm}^{-1}$ .

(ii) Preparation of 2-carbomethoxy-2-deutero-1-phenylaziridine, [4.24]

2-Carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine (0.05 g, 0.161 mmol) was placed in a 5 mm NMR tube with 0.5 ml dry deuteriochloroform under nitrogen. Dried acetone (0.023 ml, 0.318 mmol) was introduced by syringe and the tube shaken to mix the reagents. A volume of dried tetrabutylammonium fluoride corresponding to 0.1 mol equivalents was then added. NMR spectroscopy indicated immediate and complete conversion to 2-carbomethoxy-2-deutero-1-phenylaziridine, [4.24]. The sample was taken up in ether, washed with brine, dried evaporated and purified by column chromatography on silica, pentane as the eluent.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 2.24 (1 H, s,  $\text{CH}_a\text{H}_b$ ), 2.60 (1 H, s,  $\text{CH}_a\text{H}_b$ ), 3.76 (3 H, s,  $\text{OCH}_3$ ), 6.79-7.55 (5 H, m, Ph). The geminal coupling constant between the two ring protons is observed to be zero.  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) 34.4 ( $\text{CH}_2$ ), 38.1 (CD), 53.1 ( $\text{OCH}_3$ ), 121.6, 124.0, 129.5 and 152.5 (Ph), 170.1 ( $\text{C}=\text{O}$ ). Calculated M, 178.0853; measured M, 178.0731.

(iii) Fluorodesilylation of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with addition of hexanal, synthesis of 2-carbomethoxy-1-phenyl-2-(1-dimethylphenylsiloxyhexyl) aziridine, [4.1a]

2-Carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine (0.3 g, 0.965 mmol) was placed in a 2 ml teflon sealed vial which had been dried by heating. Freshly distilled hexanal (0.17 ml, 1.447 mmol) was injected into the vial. The resultant mixture was then warmed and agitated, in order to ensure thorough mixing, and then cooled to -78 °C. Tetrabutylammonium fluoride dried by method B (3 drops, *ca* 5%) were added to the vial over a 5 minute period resulting in the formation of a yellow mixture. This was allowed to warm to 0 °C and then 0.5 ml dry THF was added. After a further 17 hours at this temperature the mixture was diluted with ether, washed well with brine, dried and evaporated to give mostly the fully desilylated material and the silylether adduct (2-carbomethoxy-1-phenyl-2-(1-dimethylphenylsiloxyhexyl) aziridine) as a minor product, along with some of the free alcohol and polymerized aldehyde. The product mixture was purified by column chromatography on silica, using pentane as the eluent to give the product silylether as a colourless viscous oil (0.020 g, 0.0487 mmol, 5.0%). None of the free alcohol could be isolated from the column owing to decomposition. Preliminary investigations, attempting to desilylate the silylether to obtain the free alcohol, indicated that the product is stable to treatment with fluoride ion. Proton NMR data show that the product is present as a mixture of diastereoisomers which are denoted here as x and y. The features of the NMR spectra obtained for this product are discussed in detail in Chapter 4.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 0.313, 0.335, 0.339, 0.358 (4 x 3 H, 4 x s, Me<sub>2</sub>Si), 0.78-0.82 (3 H, 2 overlapping triplets, CH<sub>2</sub>Me<sub>x</sub> and CH<sub>2</sub>Me<sub>y</sub>), 1.20-1.66 (8 H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.28 and 2.57 (1 H, 2 x d, *J* 1.6 Hz, H<sub>xa</sub> and H<sub>xb</sub>), 2.51 and 2.64 (1 H, 2 x d, *J* 2.0 Hz, H<sub>ya</sub> and H<sub>yb</sub>), 3.18 and 3.28 (3 H, 2 x s, OMe<sub>y</sub> and OMe<sub>x</sub>), 4.14 and 4.38 (1 H, 2 x dd, *J*<sub>1x</sub> 5.8, *J*<sub>2x</sub> 8.4, *J*<sub>1y</sub> 3.2, *J*<sub>2y</sub> 8.0 Hz, HCOSi), 6.62-7.58 (10 H, m, PhN and PhSi).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) -0.6, -0.2 (SiMe<sub>2</sub>), 14.7 (CH<sub>3</sub>), 23.3 (CH<sub>3</sub>CH<sub>2</sub>), 26.3 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 32.4 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 34.1

(SiOCH<sub>2</sub>CH<sub>2</sub>), 35.2 (NCH<sub>2</sub>), 51.2 (CH<sub>3</sub>O), 52.3 (C=CO<sub>2</sub>Me), 72.2 (C=OSi). Calculated M-CH<sub>3</sub>, 396.1995; measured M-CH<sub>3</sub>, 396.2006.

(iv) Fluorodesilylation of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine with addition of benzaldehyde, synthesis of 2-carbomethoxy-1-phenyl-2-(1-dimethylphenylsiloxybenzyl) aziridine, [4.1b]

2-Carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine (0.2 g, 0.643 mmol) was placed in a 2 ml teflon sealed vial which had been dried by heating. Benzaldehyde (0.13 ml, 1.28 mmol) which had been washed with sodium sulphite and sodium bicarbonate solutions then dried and distilled, was injected into the vial. The resultant mixture was then warmed in order to ensure thorough mixing and then cooled in an ice/salt bath. Tetrabutylammonium fluoride dried by method B (2 drops, *ca* 5%) were added resulting in the formation of a brown mixture. This was maintained at 0 °C for 15 minutes and then 0.5 ml dry THF was added. After a further 0.5 hours the mixture was diluted with ether washed well with brine, dried and concentrated to give again, a silylether adduct, [4.1b] as the major product (*ca* 80% by NMR) along with some of the free alcohol and fully desilylated material. The product mixture was purified by column chromatography on silica using pentane as the eluent to give the product as a colourless viscous oil (0.150 g, 0.360 mmol, 56%). None of the free alcohol could be isolated from the column owing to decomposition. Again, preliminary investigations indicated that the product is stable to treatment with fluoride ion. The features of the NMR spectra obtained for this product are discussed in detail in Chapter 4.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 0.29 and 0.32 (2 x 3H, 2 x s, Me<sub>2</sub>Si), 2.49 and 2.73 (2 H, 2 x s, H<sub>2</sub>C<sub>x</sub> and H<sub>2</sub>C<sub>y</sub>), 3.28 and 3.31 (3 H, 2 x s, OMe<sub>x</sub> and OMe<sub>y</sub>), 5.34 and 5.60 (1 H, 2 x s, PhCH<sub>x</sub> and PhCH<sub>y</sub>), 6.64-7.91 (15 H, m, NPh, CPh, SiPh).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) -0.85, -0.33, -0.32, 1.7 (4 x CH<sub>3</sub>, SiMe), 34.5 (H<sub>2</sub>C<sub>y</sub>), 34.7 (H<sub>2</sub>C<sub>x</sub>), 51.7, 51.8, 52.2 and 52.3 (OMe<sub>x&y</sub> and MeOCOC<sub>x&y</sub>), 120.2-141.7 (14 resonances, NPh, CPh, SiPh), 150.2 and 150.7 (2 x ipso C from NPh), 168.7 and 169.1 (MeOCO<sub>x&y</sub>). Found: C, 71.38; H, 6.54; N, 2.89%, C<sub>25</sub>H<sub>27</sub>NO<sub>3</sub>Si requires: C, 71.91; H, 6.52; N, 3.35%. M/e 417 (16.3%, M<sup>+</sup>),

402 (7.4%,  $M^+ - \text{Me}$ ), 241, (46.8%,  $\text{PhC(H)OSiMe}_2\text{Ph}$ ), 167, (32.9%), 135 (100.0%,  $\text{SiMe}_2\text{Ph}$ ), 77 (18.5%).



Table 6.2 Fluorodesilylation reactions of *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine

Fluoride	Electrophile	Ratio F <sup>-</sup> :E <sup>+</sup>	Reaction conditions			Product/yield
			Solvent	Temp/°C	Time/h	
TBAF.3H <sub>2</sub> O, 1M in THF	none	1:0:1	DMSO-D <sub>6</sub>	25	24	none
TBAF.3H <sub>2</sub> O, 1M in THF	none	1:0:1	DMSO-D <sub>6</sub>	100	4	possible desilylation <sup>1</sup>
TBAF.3H <sub>2</sub> O, 1M in THF	none	0.1:0:1	DMSO-D <sub>6</sub>	25	48	none
TBAF.3H <sub>2</sub> O, 1M in THF	none	1.1:0:1	DMSO-D <sub>6</sub>	25	48	none
TBAF.3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	0.1:5:1	DMSO-D <sub>6</sub>	25	48	none
TBAF.3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	1.1:5:1	DMSO-D <sub>6</sub>	25	48	none
TBAF.3H <sub>2</sub> O (solid)	CH <sub>3</sub> COCH <sub>3</sub>	0.1:5:1	DMSO-D <sub>6</sub>	25	48	none
TBAF.3H <sub>2</sub> O (solid)	CH <sub>3</sub> COCH <sub>3</sub>	1.1:5:1	DMSO-D <sub>6</sub>	25	48	none
TBAF supported on silica gel	none	1.1:0:1	Et <sub>2</sub> O	25	24	none
TBAF supported on silica gel	none	1.1:0:1	THF	25	24	none
TBAF supported on silica gel	none	1.1:0:1	THF	65	24	none
TBAF vacuum dried, 40 °C	none	1:0:1	THF	65	72	none
TASF	PhCO <sub>2</sub> Et	1:1:1	CDCl <sub>3</sub>	25	24	none
TASF	CH <sub>3</sub> COCH <sub>3</sub>	1:1:1	CDCl <sub>3</sub>	25	24	none
KF	none	1:0:1	CD <sub>3</sub> CN	25	24	none
KF/Ph <sub>4</sub> Br (1:1)	PhCO <sub>2</sub> Et	2:1.1:1	CH <sub>3</sub> CN	50	24	none
KF/Ph <sub>4</sub> Br (1:1)	none	1:0:1	CH <sub>3</sub> CN	82	2	none
KF/Ph <sub>4</sub> Br (1:1)	none	1:0:1	CD <sub>3</sub> CN	25	24	none
KF/Ph <sub>4</sub> Br (1:1)	CH <sub>3</sub> COCH <sub>3</sub>	1:5:1	CD <sub>3</sub> CN	25	24	none
CsF	D <sub>2</sub> O (quench)	1:1:1	CH <sub>3</sub> OD	60	24	none

<sup>1</sup>NMR data indicated that desilylation may have occurred but conclusive evidence was not obtained

Table 6.3 Fluorodesilylation reactions of 1-carboethoxy-2-trimethylsilylaziridine

Fluoride	Electrophile	Ratio F <sup>-</sup> :E <sup>+</sup>	Reaction conditions			
			Solvent	Temp/°C	Time/h	Product/%yield
TBAF·3H <sub>2</sub> O, 1M in THF	none	0.1:0:1	THF	25	24	no reaction
TBAF·3H <sub>2</sub> O, 1M in THF	none	1:0:1	THF	25	48	no reaction
TBAF·3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	0.1:3:1	THF	25	24	no reaction
TBAF·3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	1:10:1	THF	25	48	no reaction
TBAF·3H <sub>2</sub> O (solid)	CH <sub>3</sub> COCH <sub>3</sub>	0.1:5:1	THF	25	48	no reaction
TBAF·3H <sub>2</sub> O (solid)	CH <sub>3</sub> COCH <sub>3</sub>	1.1:5:1	THF	25	48	no reaction
TBAF supported on silica gel	none	0.1:0:1	THF	25	24	no reaction
TBAF supported on silica gel	none	1.1:0:1	THF	25	24	no reaction
KF	none	0.1:0:1	CD <sub>3</sub> CN	25	24	no reaction
KF	none	1:0:1	CH <sub>3</sub> CN	40	24	no reaction
CsF	none	0.1:0:1	CDCl <sub>3</sub>	25	24	no reaction
CsF	none	1:0:1	CH <sub>3</sub> CN	40	24	no reaction
KF/ultrasound	none	0.1:0:1	CH <sub>3</sub> CN	30	2	no reaction
CsF/ultrasound	none	0.1:0:1	CH <sub>3</sub> CN	30	2	no reaction
KF/18-crown-6, 1%	none	1:0:1	CH <sub>3</sub> CN	25	24	no reaction
CsF/18-crown-6, 1%	none	0.1:0:1	CH <sub>3</sub> CN	25	24	no reaction
CsF/18-crown-6, 1%/ultrasound	none	0.1:0:1	CH <sub>3</sub> CN	30	2	no reaction

Table 6.4 Fluorodesilylation reactions of 2-carboethoxy-1-phenyl-2-triethylsilylaziridine

Fluoride	Electrophile	Ratio F:E+:1	Reaction conditions			Result/% yield <sup>1</sup>
			Solvent	Temp/°C	Time/h	
TBAF:3H <sub>2</sub> O, 1M in THF	none	0.1:0:1	THF	25	1	desilylated prod/70%
TBAF:3H <sub>2</sub> O, 1M in THF	none	1:0:1	THF	25	1	desilylated prod/70%
TBAF:3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	0.1:1:1	THT	25	1	desilylated prod/70%
TBAF:3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	0.1:10:1	THF	25	1	desilylated prod/70%
TBAF:3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	1:3:1	THF	25	1	desilylated prod/70%
TBAF:3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> CHO	0.1:1:1	THF	25	1	desilylated prod/70%
TBAF:3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> CHO	0.1:3:1	THF	25	1	desilylated prod/70%
TBAF:3H <sub>2</sub> O, 1M in THF	CH <sub>2</sub> CH <sub>2</sub> CHO	0.1:1:1	THF	25	1	desilylated prod/70%
TBAF:3H <sub>2</sub> O, 1M in THF	MeI	0.1:3:1	THF	25	1	no reaction
CsF	none	1:0:1	CH <sub>3</sub> CN	25	24	desilylated prod/30%
CsF	none	0.1:0:1	CH <sub>3</sub> CN	25	24	no reaction
CsF	MeI	1:1:1	CH <sub>3</sub> CN	25	24	no reaction
CsF/18-crown-6, 1%, ultrasound	CH <sub>3</sub> COCH <sub>3</sub>	1:1:1	CH <sub>3</sub> CN	30	24	desilylated prod/30%
TBAF supported on silica gel	CH <sub>3</sub> CHO	1:1:1	THF	25	7	desilylated prod/30%
TBAF (molecular sieve dried)	none	0.1:0:1	THF	25	1	desilylated prod/70%
TBAF (molecular sieve dried)	CH <sub>3</sub> CHO	0.1:1:1	THF	25	1	desilylated prod/70%

<sup>1</sup>Yields are approximate based on <sup>1</sup>H NMR data of the product after aqueous work-up.

Table 6.5 Fluorodesilylation reactions of 2-carbomethoxy-2-dimethylphenylsilyl-1-phenylaziridine

Fluoride	Electrophile	Ratio F <sup>-</sup> :E <sup>+</sup>	Reaction conditions			Result/% yield <sup>1</sup>
			Solvent	Temp/°C	Time/h	
TBAF·3H <sub>2</sub> O, 1M in THF	<i>t</i> -BuCHO	0.1:1.5:1	CCl <sub>4</sub>	25	0.1	desilylated prod./100%
TBAF·3H <sub>2</sub> O, 1M in THF	<i>t</i> -BuCHO	1:1:1	CCl <sub>4</sub>	25	0.1	desilylated prod./100%
TBAF·3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	0.1:3:1	CCl <sub>4</sub>	25	0.1	desilylated prod./100%
TBAF·3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	0.1:1:1	THF	25	0.1	desilylated prod./100%
TBAF·3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	0.1:5:1	THF	25	0.1	desilylated prod./100%
TBAF·3H <sub>2</sub> O, 1M in THF	CH <sub>3</sub> COCH <sub>3</sub>	0.1:10:1	THF	25	0.1	desilylated prod./100%
TBAF vacuum dried, 40 °C	CH <sub>3</sub> COCH <sub>3</sub>	0.2:5:1	CCl <sub>4</sub>	25	0.1	desilylated prod./100%
TBAF vacuum dried, 40 °C	MeI	0.2:5:1	THF	25	0.1	no reaction
CsF	CH <sub>3</sub> COCH <sub>3</sub>	0.2:5:1	CH <sub>3</sub> CN	25	0.1	desilylated prod./90%
CsF	<i>t</i> -BuCHO	1.1:1:1	CH <sub>3</sub> CN	25	0.1	desilylated prod./90%
TBAF (molecular sieve dried)	CH <sub>3</sub> COCH <sub>3</sub>	0.1:1:1	THF	25	0.1	desilylated prod./100%
TBAF (molecular sieve dried)	CH <sub>3</sub> COCH <sub>3</sub>	0.1:3:1	CDCl <sub>3</sub>	25	0.1	deuterated prod./100%
TBAF (molecular sieve dried)	<i>t</i> -BuCHO	0.1:1:1	none	25	0.1	no reaction
TBAF (molecular sieve dried)	<i>t</i> -BuCHO	0.1:2:1	none	25	4	no reaction
TBAF (molecular sieve dried)	PhCHO	1:1:1	THF	25	0.1	silyl ether/10%
TBAF (molecular sieve dried)	PhCHO	1:2:1	THF	25	0.1	silyl ether/80%
TBAF (molecular sieve dried)	PhCHO	1:3:1	THF	0	0.25	silyl ether/30%
TBAF (molecular sieve dried)	cyclohexanone	0.1:3:1	THF	25	0.1	desilylated prod./100%
TBAF (molecular sieve dried)	cyclohexanone	0.1:3:1	THF	0	0.1	desilylated prod./100%
TBAF (molecular sieve dried)	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> CHO	0.05:1.5:1	THF	25	0.1	desilylated prod./100%
TBAF (molecular sieve dried)	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> CHO	0.05:1.5:1	THF	-78, 0	0.25, 17	silyl ether/20%

<sup>1</sup>Yields are approximate based on <sup>1</sup>H NMR data of the product after aqueous work-up.

## 6.19 The reaction of silylaziridines with nucleophilic reagents

All of the silylaziridines synthesized during the course of this study, and some previously prepared aziridines were treated with a range of nucleophilic reagents. No nucleophilic ring cleavage reaction was successful, nevertheless, the reaction conditions are reported here since the failure of the silylaziridines to react in such a way is highly significant.

### 6.19.1 Reaction of silylaziridines with lithium dibutyl cuprate

#### (i) Reaction of 1-carboethoxy-2-trimethylsilylaziridine with lithium dibutyl cuprate

A solution of freshly dried cuprous iodide (0.76 g, 4.01 mmol) in dry ether (40 ml) under nitrogen was cooled to  $-60^{\circ}\text{C}$  and a solution (2.4M) of *n*-butyllithium in hexane (3.4 ml, 8.02 mmol) was added over a 15 minute period. The solution was then stirred for 10 minutes at  $-60^{\circ}\text{C}$  and for 30 minutes at  $-50^{\circ}\text{C}$ . Following this, the resultant red coloured mixture was cooled to  $-78^{\circ}\text{C}$  and 20 ml THF was added. After 10 minutes at this temperature, 1-carboethoxy-2-trimethylsilylaziridine (0.25 g, 1.34 mmol) was added dropwise over 10 minutes followed by stirring for 45 minutes at  $-50^{\circ}\text{C}$  before being allowed to warm slowly to room temperature. The reaction mixture was then treated with ammonium hydroxide solution and aqueous ammonium chloride. The product was then extracted with ether (3 x 20 ml portions) dried and evaporated to give quantitatively, the unreacted starting material.

#### (ii) Reaction of 1-carboethoxy-2-trimethylsilylaziridine with lithium dibutyl cuprate in the presence of boron trifluoride etherate

The above reaction (6.19.1 (i)) was repeated under the same conditions, except after generation of the cuprate reagent, the aziridine was added rapidly followed by 1 equivalent of boron trifluoride etherate. The starting material was again recovered quantitatively.

(iii) Reaction of *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine with lithium dibutyl cuprate

This reaction was carried out by the method described in 6.17.1 (i) using 1.49 g (7.85 mmol) cuprous iodide, a hexane solution of *n*-butyllithium (9.8 ml, 1.6*M*, 15.7 mmol) and *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine (0.5 g, 2.62 mmol). The starting aziridine was recovered quantitatively.

(iv) Reaction of *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine with lithium dibutyl cuprate in the presence of boron trifluoride etherate

The above reaction (6.18.1 (iii)) was repeated under the same conditions except after generation of the cuprate reagent, the aziridine was added rapidly followed by 1 equivalent of boron trifluoride etherate. No starting material remained but a mixture of products was obtained that could not be identified.

#### 6.19.2 Reactions of silylaziridines with methyl iodide

All of the aziridines synthesized during the course of this study were treated with neat methyl iodide at reflux or at 40 °C in dioxane for several days. No reaction what ever was observed in any case.

#### 6.19.3 Reactions of 1-carboethoxy-2-trimethylsilylaziridine with amines

(i) Reaction of 1-carboethoxy-2-trimethylsilylaziridine with aniline

1-Carboethoxy-2-trimethylsilylaziridine (0.2 g, 1.07 mmol) and aniline (0.12 g, 1.28 mmol) were heated together in the absence of solvent at 110 °C for 8 hours. The starting material remained completely unreacted after this period.

(ii) Reaction of 1-carboethoxy-2-trimethylsilylaziridine with aniline in the presence of ethanol

1-Carboethoxy-2-trimethylsilylaziridine (0.2 g, 1.07 mmol) and aniline (0.12 g, 1.28 mmol) were dissolved in ethanol (10 ml) and the solution was heated at reflux for 4 days. The starting materials were recovered quantitatively after this period.

(iii) Reaction of 2-carbomethoxy-1-phenyl-2-triethylsilylaziridine with benzylamine in the presence of alumina

2-Carbomethoxy-1-phenyl-2-triethylsilylaziridine (0.1 g, 0.344 mmol) was dissolved in 5 ml dioxane and benzylamine (0.037 g, 0.346 mmol) and neutral alumina (1.0 g) were added. The mixture was stirred at reflux for 24 hours, filtered and evaporated to give the starting material quantitatively.

(iv) Reaction of 1-carboethoxy-2-trimethylsilylaziridine with benzylamine in the presence of ethanol

1-Carboethoxy-2-trimethylsilylaziridine (0.15 g, 0.802 mmol) and benzylamine (0.103 g, 0.963 mmol) were dissolved in ethanol (5 ml) and the solution was heated at reflux for 4 days. The starting materials were recovered completely unreacted after this period.

6.19.4 Reactions of 1-carboethoxy-2-trimethylsilylaziridine with diethyl malonate anion

1-Carboethoxy-2-trimethylsilylaziridine was treated with the diethyl malonate anion under the conditions described below. The reaction was repeated using THF or DMF as the solvent, and also in ethanol using sodium ethoxide as the base. Further experiments were conducted using a two fold excess of the malonate anion and also heating the reaction

mixture at reflux for 16 hours prior to work-up. The reaction using ethoxide as the base was refluxed for 24 hours prior to work-up.

Diethyl malonate (0.14 g, 0.85 mmol) was dissolved in 5 ml of dry ether and sodium hydride (0.020 g, 0.85 mmol) added, causing effervescence, and the mixture stirred for 0.5 hours. 1-Carboethoxy-2-trimethylsilylaziridine (0.15 g, 0.80 mmol) was added resulting in the development of a deep yellow colour and the now flocculant mixture stirred for 4 hours at ambient temperature, or in the case where DMF was used as the solvent, at 90 °C for 4 days. Dilute hydrochloric acid was added and the organic layer washed with brine, dried and evaporated. The starting aziridine was recovered unreacted.

#### 6.19.5 Reactions of silylaziridines with methyl magnesium iodide

##### (i) Reactions of 1-carboethoxy-2-trimethylsilylaziridine with methyl magnesium iodide

1-Carboethoxy-2-trimethylsilylaziridine (0.1 g, 0.535 mmol) was dissolved in 1 ml dry ether and 0.7 ml (0.58 mmol) of methyl magnesium iodide in ether (0.822 M) was added. The mixture was stirred at room temperature for 6 hours prior to aqueous work-up. The starting aziridine was recovered quantitatively.

##### (ii) Reaction of *cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine with methyl magnesium iodide

*Cis*-3-phenyl-1-propyl-2-trimethylsilylaziridine (0.1 g, 0.429 mmol) was dissolved in 1 ml dry ether and 1.3 ml (1.06 mmol) of methyl magnesium iodide in ether (0.822 M) was added. The mixture was stirred at room temperature for 6 hours prior to aqueous work-up. The starting aziridine was recovered quantitatively.



## 6.20 The synthesis of vinylsilanes by the reaction of carbonyl compounds with $\alpha$ -lithiovinyltrimethylsilane

Ethyl chloroformate, acetyl chloride, acetic anhydride, ethyl acetate, phenylchloroformate and dimethylcarbamyl chloride were reacted with  $\alpha$ -lithiovinyltrimethylsilane. Identical reaction conditions were used in each case. The general procedure is described for the reaction with ethyl chloroformate. The reaction with phenyl chloroformate led to a mixture of products and so the results have not been included.

All of the NMR spectra obtained in this study were recorded on a 400 MHz instrument.

### (i) Preparation of 4,4,4-tricarboethoxy-2-trimethylsilylbut-1-ene. [5.21]

A solution of  $\alpha$ -bromovinyltrimethylsilane (3.04 g, 0.017 mol) in THF (50 ml) was cooled to  $-110\text{ }^{\circ}\text{C}$  with stirring under nitrogen. *t*-Butyllithium in pentane (11.2 ml, 0.019 mol) was added dropwise over 10 minutes, maintaining the temperature below  $-100\text{ }^{\circ}\text{C}$  throughout. The bright yellow solution was stirred for a further 30 minutes at  $-100\text{ }^{\circ}\text{C}$  then cooled to  $-110\text{ }^{\circ}\text{C}$ . Ethyl chloroformate was added dropwise over 10 minutes and the temperature maintained at  $-110\text{ }^{\circ}\text{C}$  for a further 20 minutes. The mixture was then allowed to warm slowly to room temperature and stirred for an additional 17 hours. Hydrolysis at  $0\text{ }^{\circ}\text{C}$  with saturated ammonium chloride solution was followed by extraction with ether and drying. The product was purified by flash column chromatography.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 0.15 (9 H, s,  $\text{Me}_3\text{Si}$ ), 1.29 (9 H, q, 3 x  $\text{CH}_2\text{CH}_3$ ), 3.02 (2 H, s,  $\text{CH}_2\text{C}(\text{CO}_2\text{Et})$ ), 4.25 (6 H, t, 3 x  $\text{CH}_2\text{CH}_3$ ), 5.48 (1 H, s,  $\text{H}_a\text{H}_b\text{C}=\text{}$ ), 5.69 (1 H, s,  $\text{H}_a\text{H}_b\text{C}=\text{}$ ). (The geminal coupling constant between  $\text{H}_a$  and  $\text{H}_b$  is observed to be zero.)  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) -0.8 ( $\text{Me}_3\text{Si}$ ), 14.8 ( $\text{CH}_3$ ), 37.6 ( $\text{CH}_2\text{CSi}$ ), 62.8 ( $\text{CH}_2\text{O}$ ), 66.5 ( $\text{C}(\text{CO}_2\text{Et})_3$ ), 127.3 ( $\text{H}_2\text{C}=\text{}$ ), 147.0 ( $\text{CSiMe}_3$ ), 167.5 ( $\text{C}=\text{O}$ ).  $\delta_{\text{Si}}$  ( $\text{CDCl}_3$ ) -52.73.  $\nu_{\text{max}}$ . 2983-2961, 1745 (str.), 1298, 1256, 1218, 1064 and  $844\text{ cm}^{-1}$ . Found C, 55.83; H, 8.56%,  $\text{C}_{16}\text{H}_{28}\text{O}_6\text{Si}$  requires C, 55.79; H, 8.19%.  $\text{M/e}$  345 (20.6%,  $[\text{M}+\text{H}]^+$ ), 329 (66.1%,  $\text{M}-\text{Me}$ ), 257 (44.4%,  $\text{CH}_2\text{C}(\text{CO}_2\text{Et})_3$ ), 227 (43.2%), 211 (70.0%), 197 (29.6%), 183 (41.7%), 181 (36.8%), 153 (39.8%), 75

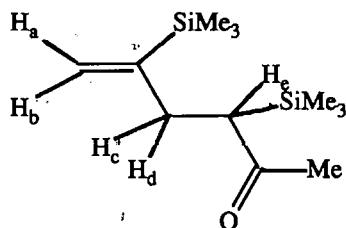
(47.4%), 73 (100.0%, CO<sub>2</sub>Et or SiMe<sub>3</sub>), 29 (78.8%, Et). Calculated M-CH<sub>3</sub>, 329.1420; measured M-CH<sub>3</sub>, 329.1421.

(ii) 2-Acetoxy-3,5-bis(trimethylsilyl)hexa-2,5-diene, [5.22]

When the reaction was carried out using acetic anhydride as the quenching agent, 2-acetoxy-3,5-bis(trimethylsilyl)hexa-2,5-diene was obtained in 84.6% yield after purification. The product could be identified since it had already been made by Brook and Duff<sup>10</sup>, by the action of  $\alpha$ -trimethylsilylvinylmagnesium bromide on acetic anhydride. This product was also obtained using acetyl chloride as the quenching reagent, however, the product mixture was much less pure and no attempts were made to isolate the components.  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) [0.03 (9 H, s); and 0.08 (9 H, s) 2 x Me<sub>3</sub>Si], 1.96 (3 H, s, MeC=C), 2.08 (3 H, s, MeC=O), 2.74 (2 H, s, CH<sub>2</sub>), 5.22 (1 H, d, *J* 2.4 Hz, H<sub>a</sub>H<sub>b</sub>C=), 5.38 (1 H, m, H<sub>a</sub>H<sub>b</sub>C=).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) -3.6 and -3.3 (2 x Me<sub>3</sub>Si), 20.0 (MeC=C), 20.8 (MeC=O), 33.8 (CH<sub>2</sub>), 120.3 (MeC=C), 123.3 (H<sub>2</sub>C=C), 149.2 (MeC=C), 151.7 (H<sub>2</sub>C=C), 168.7 (C=O).

(iii) 3,5-Bis(trimethylsilyl)hex-5-en-2-one, [5.24]

When the quenching agent was ethyl acetate, 3,5-bis(trimethylsilyl)hex-5-en-2-one, [5.24] was produced.



$\delta_{\text{H}}$  (CDCl<sub>3</sub>) [0.10 (3 H, s); and 0.11 (3 H, s) 2 x Me<sub>3</sub>Si], 2.04 (3 H, s, CH<sub>3</sub>), 2.19 (1 H, dd, H<sub>c</sub>), 2.67-2.75 (2 H, m, H<sub>d</sub> and H<sub>e</sub>), 5.27 (1 H, s, H<sub>a</sub>), 5.47 (1 H, s, H<sub>b</sub>).  $\delta_{\text{C}}$

(CDCl<sub>3</sub>), -2.5 and -1.5 (2 x Me<sub>3</sub>Si), 31.6 (CH<sub>3</sub>), 32.6 (CH<sub>c</sub>H<sub>d</sub>), 47.6 (CH<sub>e</sub>), 123.7 (CH<sub>a</sub>H<sub>b</sub>), 151.4 (SiC=), 209.3 (C=O).

(iv) 1-Dimethylamido-1,3-bis(trimethylsilyl)but-3-ene, [5.23]

1-Dimethylamido-1,3-bis(trimethylsilyl)but-3-ene was isolated from the product mixture when dimethylcarbonyl chloride was used as the quenching agent. The dark green reaction mixture on work-up offered a dark brown oil. On cooling in an acetone/cardice bath a dark brown solid precipitated (NMR spectra suggested presence of mostly *N*-methyl groups). This procedure was repeated several times and the mother liquor concentrated to give the product which was substantially contaminated with hydrocarbon material. The product was obtained pure by column chromatography on silica, using hexane as the eluant. Yield after purification, 6.6%.  $\delta_C$  (CDCl<sub>3</sub>) -1.76 and -0.83 (2 x Me<sub>3</sub>Si), 32.20 (CH<sub>3</sub>), 32.8 (CH<sub>2</sub>CHCO), 48.3 (CHCO), 124.2 (H<sub>2</sub>C=), 152.1 (SiCH=), 209.9 (C=O). Found C, 55.99; H, 10.61; N, 4.17%, C<sub>13</sub>H<sub>29</sub>NSi<sub>2</sub>O requires C, 57.50; H, 10.76; N, 5.16%.  $\nu_{\max}$ . 2810-3115, 1635, 1395, 1250, 1135, 1040, 915, 848, 740 and 665 cm<sup>-1</sup>. M/e 271 (10.2%, M<sup>+</sup>), 256 (22.1%, M<sup>+</sup>-Me), 227 (6.2%, M<sup>+</sup>-NMe<sub>2</sub>), 198 (75.0%, M<sup>+</sup>-SiMe<sub>3</sub>), 172 (43.5%, CH<sub>2</sub>CH(SiMe<sub>3</sub>)CONMe<sub>2</sub>), 147 (20.5%), 73 (100.0%, SiMe<sub>3</sub>).

6.21 Preparation of 4,4,4-tricarboethoxy-2-trimethylsilylbut-1-ene, [5.21]  
by a Grignard route

Magnesium turnings (1.49 g, 61.4 mmol) were stirred for 10 minutes under nitrogen and then 20 ml THF was added. The solvent was then heated to reflux and addition of  $\alpha$ -bromovinyltrimethylsilane (11.0 g, 61.4 mmol) was begun. A vigorous reaction ensued after the first few drops of the bromide had been added. This was followed by the addition of 10 ml of THF in one portion and the remaining  $\alpha$ -bromovinyltrimethylsilane (in an equal volume of THF) dropwise. The mixture was heated to reflux for 30 minutes and then cooled in an ice bath. Ethyl chloroformate (10.0 g, 92.1 mmol) was added dropwise to the cooled Grignard reagent and the mixture was stirred for a further 5 minutes. The mixture was then gently refluxed for 2 hours. Following cooling in an ice bath, it was diluted with

ether (100 ml) and hydrolysed by addition of water (10 ml). The resultant mixture was filtered, and the filtrate washed with brine, dried and evaporated to give (by comparison with an authentic sample), 4,4,4-tricarboethoxy-2-trimethylsilylbut-1-ene (8.15 g, 23.7 mmol, 77%) in an almost pure form.

## 6.22 References

1. H. Gilman, F. Cartledge and S.Y. Sim, *J. Organomet. Chem.*, **1**, 8, (1963).
2. M. O. Forster and H. E. Fierz, *J. Chem. Soc.*, **93**, 81, (1908).
3. R.A. Benkeser and R.A. Hickner, *J. Amer. Chem. Soc.*, **80**, 5298 (1958).
4. E. Lukevics in 'Frontiers of organosilicon chemistry', Ed. A.R. Bassindale and P.P. Gaspar, The Royal Society of Chemistry, Cambridge, 1991, p 383.
5. A. Ottolenghi, M. Fridkin and A. Zilkha, *Can. J. Chem.*, **41**, 2977, (1963).
6. M.C.C. Soobramanien, Ph.D. Thesis, The Open University, Milton Keynes, (1988).
7. R.O. Lindsay and C.F.H. Allen, Organic Syntheses, Collective Volume 3, John Wiley and Sons, Inc., New York, 1967, p. 710.
8. F. Duboudin and O. Laporte, *J. Organomet. Chem.*, **156**, C 25-28, (1978).
9. D.P. Cox, J. Terpinski and W. Lawrynowicz, *J. Org. Chem.*, **49**, 3216, (1984).
10. A.G. Brook and J.M. Duff, *Can. J. Chem.*, **51**, 2024, (1973).